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VALUE AND DURATION OF IMMUNITY CONFERRED BY ANTIDIPHTHERITIC ANATOXIN

TITRATION OF ANTITOXIN PRESENT IN THE SERUM OF VACCINATED CHILDREN *

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It is a familiar fact that after three injections of antidiphtheritic anatoxin, properly made, a Schick reaction that is positive before vaccination becomes negative in about 95 per cent of the cases. The Schick test, however, which is useful in practice, shows only whether the serum does or does not contain a proportion of specific antitoxin corresponding to one thirtieth of an Ehrlich unit, this proportion being thus far considered as necessary and sufficient for protecting man against a toxic injection determined by the diphtheria bacillus. Interest is not lacking, however, in additional information concerning the exact value of the immunity produced by anatoxin and the fluctuations that this immunity may undergo during the years following vaccination. As soon as one of us (G. R.) suggested anatoxin for the active immunization of man against diphtheria (1923), Martin,[1] Darré, Loiseau and A. Laffaille showed, by determinations of the antitoxin present in the serum of about ten persons, that the injection of anatoxin is capable of causing in man, as well as in animals, an abundant production of specific antitoxin.

We thought that it would be useful to extend this problem and to examine it closely. We therefore undertook to determine, by means of strict technic, the diphtheritic antitoxin content of the serum of a sufficient number of children vaccinated against diphtheria by the injection of anatoxin, the vaccination dating from periods of one to five years.

This study was completed at the Maritime Hospital at Berck, France,

* Submitted for publication, July 18, 1930.
* From the Institut Pasteur.
* Translated by Theodore C. Merrill, M.D., Paris.
1. Martin, L.: Bull. Acad. de méd. 91:523, 1924.

through the courtesy of our colleague, Dr. Sorrel, chief of this service. The situation there is especially favorable for a study of this kind. Children under treatment remain hospitalized for a prolonged period, during which they are completely studied clinically and biologically. The history of their condition becomes well known, and incidents occurring during their stay at the Maritime Hospital (for example, contact with persons affected with diphtheria) are noted carefully. At this hospital, antidiphtheritic vaccination with anatoxin, which was begun in December, 1925, is now systematically practiced on all the children by M. Mozer and G. Mozer, who have observed its remarkable effects on endemic diphtheria.[2]

We thus know, for every child and in a precise manner, the exact quantities of anatoxin injected, the dates of injection and, in a large number of cases, the result of the Schick test before vaccination. By means of these valuable preliminary studies, it has been possible to make our investigations under exact conditions.

The results are in no way modified by the fact that most of the children studied presented tuberculosis. All the children whom we selected were in an excellent general condition. Observations made on them are fully comparable with those made on a certain number of children hospitalized for nontuberculous conditions, such as rachitis or osteomyelitis.

The technic that we adopted is directly derived from the fundamental technic of Ehrlich. We believe that it supplies a maximum of precision in the titration of antitoxin present in the blood.[2] One of us (G. R.) has already fruitfully utilized it, especially in the course of studies pursued in collaboration with Zoeller.

We made complete determinations of this kind with the serum of 105 children. To show the results obtained, we shall describe: (1) the relation between the antitoxin content of the serum and the result of the Schick test, (2) the influence of the number of injections of anatoxin on the antitoxin content of the serum, (3) the influence of the age of the child when vaccinated, (4) the influence of contact with persons affected with diphtheria and (5) the influence of the duration of the period following vaccination, permitting determination of the duration of immunity.

RESULTS

The Antitoxin Content of the Serum and the Schick Reaction.— Titration of the antitoxic power of the serums of the 105 children tested showed antitoxic power above 1 unit in 43 (40.9 per cent), above one-tenth unit in 52 (49.2 per cent), above one-thirtieth unit in 6 (5.7 per cent) and below one-thirtieth in 4 (3.8 per cent).

2. This technic is fully described in a paper by us, in Ann. de l'Inst. Pasteur **45**:326 (Sept.) 1930.

The high content of antitoxin in the serum is well shown by the fact that 90.1 per cent of the children had an antitoxic capacity higher than one-tenth unit, and that a capacity above one-thirtieth unit existed in 96 per cent.

The Schick test was negative in 101 (96.2 per cent) of the 105 children and positive in 4. In the 4 cases presenting a positive Schick reaction after vaccination, the antitoxic power was below one-thirtieth unit. Contrary to certain observations, which we do not consider acceptable, our experience confirms the opinion that the negative Schick test corresponds with a serum the antitoxin content of which is higher than one-thirtieth unit.

Our experience further shows that vaccination with anatoxin permits the immunization of more than ninety-six children per hundred, if it be granted that a person who gives a negative Schick reaction and whose serum contains more than one-thirtieth antitoxic unit is protected against diphtheria or, at all events, against a grave attack of diphtheria. This proportion is in agreement with that previously established by writers who have employed and tested anatoxin. Finally, this proportion shows that the serum of nine of ten subjects vaccinated with anatoxin has antitoxic power above one-tenth unit; consequently, their immunity is well established and will endure.

It is somewhat difficult to compare these results with those of similar studies made in France or other countries. In fact, there has been no other employment of the strict technic indicated at the beginning of this paper and devised for titrating the antitoxin present in the serum of children vaccinated against diphtheria. We find few studies comparable with the present one, even when considering writers who have employed the usual Römer method of determination. For children vaccinated with anatoxin, the only studies which have thus far appeared are those made, as we have mentioned, by Martin and by Loiseau, Darré and Laffaille, to which should be added a study by Maloney and Fraser of Toronto. Studies made by these writers permit precise appreciation of the value of the immunity conferred by anatoxin.

For children vaccinated with the tuberculin or the albumose-free tuberculin mixtures, excluding the initial researches made by Behring, the most important contributions have been made by Rohmer and Lévy of Strasbourg. With these should be included the older study by Gorter and Ten Brokkel Huininck and the more recent publications by Porkels of Hamburg. A study of these contributions shows that the serums of children vaccinated with the tuberculin and the albumose-free tuberculin mixtures contain, as an almost absolute rule, quantities of antitoxin that are far inferior to those found in children vaccinated with anatoxin. It shows, besides, that the number of children not immunized by this vaccination is distinctly larger than that after one employs vaccination with anatoxin.

The Influence of the Number of Injections on the Antitoxin Content of the Serum.—Thirty-seven of the children vaccinated at Berck in 1925 received only two injections of anatoxin. The results obtained showed antitoxic power above 1 unit in sixteen (43.24 per cent), above one-tenth unit in nineteen (51.08 per cent), above one-thirtieth unit in one (2.8 per cent) and below one-thirtieth unit in one (2.8 per cent).

From the beginning of 1926, the children received three injections. We studied sixty-eight of this group, obtaining the following results: antitoxic power above one unit in twenty-seven (39.4 per cent), above one-tenth unit in thirty-four (50 per cent), above one-thirtieth unit in four (5.88 per cent) and below one-thirtieth unit in 3 (4.44 per cent).

The slight difference in the results obtained in children vaccinated but twice, in 1925, and those obtained in children vaccinated three times, since 1926, must be attributed to a difference in the postvaccinal period. On the one hand, a slight diminution of antitoxic power following artificial immunization intervenes and, on the other, there is a spontaneous increase in the antitoxic capacity of certain subjects in contact with the diphtheria bacillus (the phenomenon of occult immunization). A compensatory condition or status thus appears to become established between these two processes, giving rise to the same level of antitoxin observed in the two groups of vaccinated children described.

The results in five children who had previously been vaccinated and in whom the Schick reaction remained positive until 1928 require separate examination. In 1928, these children received further injections of anatoxin. Four received a fourth injection of 1.5 cc. and the fifth an entire new series of vaccinations, consisting of 0.5, 1 and 1 cc. of anatoxin at the usual intervals. When last observed, these children presented negative Schick reactions and a high antitoxic capacity. In two cases, the antitoxic power of the serum was over 1 unit and in the other three cases over 0.1 unit.

With this series we group the two children who received only three injections, with an interval of fifteen months between the first and second injection in one case, and with an interval of thirteen months between the second and third injection in the other. The antitoxic content of the serum was high in both cases, the antitoxic power being more than 1 unit and less than 3 units.

These facts show the utility and high value of a fourth injection for children not successfully vaccinated by the usual series of three injections of anatoxin, and they also prove the usefulness of prolonged intervals between two of the injections. They suggest that the results obtained experimentally by Glenny and one of us (G. R.) should be grouped with the interesting observations already made by Gorter and Ten Brokkel Huininck, of Leyden, in vaccinating with the toxin-

antitoxin mixture, and they agree with the ideas presented by Zoeller and one of us (G. R.) on "acquired reactivity" and on the practice of a recalling or supplementary injection given for increasing the immunity produced in man by antidiphtheritic and antitetanic anatoxins.

The Influence of Age on the Result of Vaccination.—We grouped the children studied into three classes, on the basis of age, as follows: between 3 and 6 years, between 6 and 10 years and over 10 years. Children below 6 years of age when examined showed: antitoxic power above 1 unit in nine (31 per cent), above one-tenth unit in seventeen (58.6 per cent), above one-thirtieth unit in two (7 per cent) and below one-thirtieth unit in one (3.4 per cent). Children between 6 and 10 years of age when examined showed: antitoxic power above 1 unit in twenty-two (40 per cent), above one-tenth unit in twenty-nine (52 per cent), above one-thirtieth unit in two (3.6 per cent) and below one-thirtieth unit in two (3.6 per cent). Children over 10 years of age when examined showed: antitoxic power above 1 unit in twelve (57.1 per cent), above one-tenth unit in seven (33.3 per cent), above one-thirtieth unit in one (4.7 per cent) and below one-thirtieth unit in one (4.7 per cent).

These results show that the older the child was when vaccinated, the higher the percentage of the antitoxin content of the serum. In children vaccinated before the age of 6 years, the antitoxic value of the serum was higher than 1 unit in 31 per cent; in those vaccinated between the sixth and tenth years, the same value of the serum occurred in 40 per cent, and in those vaccinated when more than 10 years of age, it was present in 57 per cent.

These differences are probably due to the fact that the number of children presenting negative Schick reactions increases with age and that a higher antitoxin content of the serum is obtained by vaccinating children with negative Schick reactions than by vaccinating those whose Schick reactions are positive. Again, children who are not very young may give positive Schick reactions and have serums containing larger quantities of antitoxin (although below one-thirtieth unit) than is the case with very young children, owing to the beginning of occult immunization. It is also clear that in these three series of children of various ages, the same small number of children refractory to immunization exists.

The Influence of Contact with Persons Affected with Diphtheria.—It may be inquired whether contact with persons affected with diphtheria may not increase the immunity present in vaccinated children, and whether this increase in immunity may not appear as an increased antitoxin content of the serum. We therefore carefully investigated such contacts among our subjects. It was found that, since vaccination, forty-

seven children had been in contact with patients with diphtheria. In several cases, contact of this kind had been repeated five or six times during the hospitalization period at the Berck Maritime Hospital. In these forty-seven children, examination showed: antitoxic power above 1 unit in eighteen (38.2 per cent), above one-tenth unit in twenty-five (53.2 per cent), above one-thirtieth unit in three (6.3 per cent) and below one-thirtieth in one (2.1 per cent).

On the other hand, results were as follows in a group of fifty-eight children not in contact with patients with diphtheria: antitoxic power above 1 unit in twenty-five (43.1 per cent), above one-tenth unit in twenty-eight (48.3 per cent), above one-thirtieth unit in two (3.4 per cent) and below one-thirtieth unit in three (5.1 per cent).

This study appears to show that contact with persons affected with diphtheria does not modify the antitoxin content of the serums of vaccinated children. In fact, such contacts may have occurred without our knowledge; also, diphtheria bacilli were diffused about our patients and doubtless vegetated in healthy germ-carriers among the patients and nurses at the Maritime Hospital. It is therefore difficult to draw formal conclusions in this respect from our study.

The Influence of the Postvaccinal Period on the Present Antitoxin Content of the Serum.—Of the children studied, thirty-nine were vaccinated in 1925 (a postvaccinal period of more than four years), eighteen were vaccinated in 1926 (a postvaccinal period of more than three years), twenty-six were vaccinated in 1927 (a postvaccinal period of more than two years) and twelve were vaccinated in 1928 (a postvaccinal period of more than one year). The antitoxin content of the serum of the children belonging to these four groups is as follows. The group with a postvaccinal period of more than four years showed: antitoxic power above 1 unit in seventeen (43.85 per cent), above one-tenth unit in twenty (51.5 per cent), above one-thirtieth unit in one (2.5 per cent) and below one-thirtieth unit in one (2.5 per cent). Those with a postvaccinal period of more than three years showed: antitoxic power above 1 unit in five (31.25 per cent), above one-tenth unit in ten (66.66 per cent), above one-thirtieth unit in one (5.55 per cent) and below one-thirtieth unit in none. The children with a postvaccinal period of more than two years showed: antitoxic power above 1 unit in twelve (33.33 per cent), above one-tenth unit in twenty (55.5 per cent), above one-thirtieth unit in two (5.5 per cent) and below one-thirtieth unit in two (5.5 per cent). Those with a postvaccinal period of more than one year showed: antitoxic power above 1 unit in eight (66.66 per cent), above one-tenth unit in two (16.6 per cent), above one-thirtieth unit in one (8.3 per cent) and below one-thirtieth unit in one (8.3 per cent).

The results we obtained may be summarized as follows: 1. Even when the postvaccinal period was more than four years, a small number of subjects (2.5 per cent) presented no protective immunity. 2. It is evident that among the patients with sufficient immunity, those whose serum had a high antitoxin content (with antitoxic power above one-tenth unit) included: 95 per cent of those with a postvaccinal period of more than four years, 95 per cent with a postvaccinal period of more than three years, 89 per cent with a postvaccinal period of more than two years and 82 per cent with a postvaccinal period of more than one year. These figures show in the clearest manner possible that the antitoxin content of the serum does not diminish with time, and they constitute a weighty argument in favor of a fact of capital importance, namely, the persistence, without diminution, of the immunity obtained by the use of anatoxin in vaccination against diphtheria.

DIPHTHERIA IMMUNIZATION

THE PERCUTANEOUS METHOD OF LOEWENSTEIN *

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At the present time, toxin-antitoxin is undoubtedly the most popular agent in America for producing an active immunity against diphtheria. The original preparation, first recommended by von Behring [1] in 1913, was an underneutralized mixture of toxin and antitoxin, so combined that tests made on guinea-pigs showed a slight excess of toxin. Von Behring worked on the hypothesis that the slight excess of toxin had an immunizing action. This theory, however, was disproved by Park,[2] who showed the immunizing effect of fully neutralized mixtures of toxin-antitoxin, and also by Loewenstein and Bousson,[3] who used overneutralized mixtures. The latter investigators showed, further, that immunity produced by the use of toxin-antitoxin mixtures develops later than the immunity induced by the use of free toxin. They concluded that a dissociation of the combination of toxin and antitoxin took place in the body, and that the toxin which was gradually liberated stimulated the production of immune bodies.

Hundreds of thousands of children have been treated with mixtures of toxin-antitoxin, especially in America, where a high percentage of negative control Schick tests have been reported—from 68.7 to 98 per cent by Park and Zingher.[4] An occasional death from the use of toxin-antitoxin has been reported, though the number is insignificant as compared with the thousands of children who have been successfully immunized without deleterious effects.

On the injection of the original von Behring toxin-antitoxin very unpleasant reactions occurred, especially in older children. This was

* Submitted for publication, July 18, 1930.

* From the Dept. of Pediatrics, Northwestern University, School of Medicine.

1. von Behring, E. A.: Gesammelte Abhandlungen, Bonn, A. Moreus and E. Webers, Verlag, 1915.

2. Park, W. H.: Toxin Anti-Toxin Immunization Against Diphtheria, J. A. M. A. **79**:1584 (Nov. 4) 1922.

3. Loewenstein, E., and Bousson; Zentralbl. f. Bakteriol. **86**:572, 1921.

4. Park, W. H., and Zingher, A.: Immunity Results Obtained with Diphtheria Toxoid and One-Tenth L+ Mixtures of Toxin-Antitoxin in Public Schools of New York City, Am. J. Dis. Child. **28**:464 (Oct.) 1924.

partially overcome by the use of neutralized or overneutralized mixtures. Such preparations were not tolerated by children suffering from any form of tuberculosis. It is believed by reliable investigators that toxin-antitoxin should not be used for children suffering from active tuberculosis.

For the past several years preparations of toxin-antitoxin obtained by inoculating either sheep or goats with toxin have been introduced. It was the purpose of these preparations to minimize the occurrence of reactions that frequently followed the use of horse serum, and to guard against sensitization. It is obvious that the use of the sheep or the goat serum would permit the administration of diphtheria or tetanus antitoxin, usually prepared from horse serum, if necessity arose at a subsequent period. The hopes held for the sheep and the goat preparations have not been fully realized, for not infrequently unpleasant serum reactions have been encountered following the injection of these products.

Another unsatisfactory feature more recently ascribed to the action of toxin-antitoxin is the increase of cases of diphtheria during the first six weeks following the injection. This point has been emphasized particularly by Finkelstein [5] and by Hamburger [6] and his pupils, Siegl [7] and Loewenstein.[8] The increased incidence of diphtheria during this period has been explained by the so-called "negative phase." The negative phase is a temporary decrease in immunity, and, as has been recently shown by Basch, it develops in from six to twelve days following the beginning of the injection and has a duration of from six to eighteen days.

Because of the unsatisfactory results with toxin-antitoxin, many investigators have attempted to develop a more efficient product. The earliest development was toxin-antitoxin flocculent (T.A.F.), suggested by Ramon and applied by Schmidt. This product is not available for use in this country. Diphtheria toxoid (anatoxin), however, has found a more widespread use. This anatoxin recommended by Loewenstein and perfected by Ramon, is made by the addition of formaldehyde to toxin with the application of heat. The formaldehyde tends to render innocuous the diphtheria toxin. Since it contains no free horse serum, its use would be advantageous, because immunity may be produced without producing sensitization to horse serum and without the administration of free toxin. But, on the other hand, the severe local and general reactions that may occur with the use of anatoxin have deterred many clinicians from the general employment of this substance.

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5. Finkelstein: Verhandl. d. Kinderaerzte-Kongress in Wiesbaden, 1929.

6. Hamburger and Haidvogl: Arch. f. Hyg. **98**:108, 1927.

7. Siegl, J.: Arch. f. Kinderh. **88**:95, 1929.

8. Loewenstein, E.: Klin. Wchnschr. **8**:2283, 1929; Wien. klin. Wchnschr. **42**:193, 1929; Deutsche med. Wchnschr. **55**:53, 1929.

Since July, 1929, we have used the percutaneous method of Loewenstein for producing an active immunity against diphtheria in sixty-two children of various ages. The material [9] used was Loewenstein's ointment, kindly supplied to us from his laboratory. This preparation contains not only diphtheria toxoid, but also the unfiltered, full culture of dead diphtheria bacilli incorporated into an ointment. This culture is included by Loewenstein in the ointment in order to produce an antibacillary action, which, he believed, is essential to secure absolute immunity against diphtheria.

TECHNIC

Either the back, the chest and abdomen or the arms can be used as the site for the rub. The choice in each case depends on the size of the child. In smaller children the arms do not offer a sufficiently large absorbing surface, so that either the back or the chest and the abdomen should be used. The skin is prepared with ether to remove the natural body oils and scales. This is followed by the application of alcohol, which is allowed to dry. The contents of a single tube containing the preparation are applied and rubbed in, either the finger tips or a small wooden spatula being used. This takes from about two to three minutes. The ointment dries shortly, leaving a yellow coating resembling in appearance dried glue or shellac. The surface is not washed for twenty-four hours.

RESULTS

Twenty of our group were children from a Chicago orphanage. The remaining forty-two were made up of patients encountered in private practice. The group included children of both sexes, ranging in age from 11 months to 17 years. Every member of this group had a preliminary Schick test, which was positive. Three rubs were given at weekly intervals, and, after variable periods as indicated in the tables, control Schick tests were made.

As our tables indicate, 62 children were treated with Loewenstein's ointment. Of this number, 44 children, or 70.9 per cent, showed negative control Schick tests after variable periods. This percentage agrees with the results obtained by Baar and Grabenhofer [10] who treated 26 children. Loewy [11] was the first to use the Schick test as a control before and after treatment with Loewenstein's ointment. Her results on 500 children showed 68 per cent negative Schick tests.

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9. From July, 1929, to January, 1930, we employed Loewenstein's original experimental salve which was provided in 10 cc. glass bottles. Since January, 1930, Professor Loewenstein has sent us tubes containing single doses of the refined salve.

10. Baar, H., and Grabenhofer, A.: Ueber percutane Immunisierung gegen Diphtherie nach Loewenstein, Wien. klin. Wchnschr. **42**:950, 1929; Ztschr. f. Kinderh. **48**:248, 1929.

11. Loewy, L.: Diphtherieschutzimpfung mit der Löwensteinschen Toxoidsabel, Wien. klin. Wchnschr. **25**:1415, 1929.

These percentages for the percutaneous method compare favorably with the figures reported for the toxin-antitoxin mixture. American investigators reported from 68.7 to 98 per cent (average 83 per cent) negative results with the Schick test after the administration of toxin-antitoxin. In most of the cases in which the higher percentages are reported, the children were not controlled by a Schick test prior to the

TABLE 1.—*Cases from General Practice; Group I*

Case	Age, Months	Schick Test	Months After Last Rub
1	11	+	6½
2	13		4
3	14		4
4*	17		5½
5	18		4½
6	18		6
7	19		5½
8	19		5½
9	19		4
10	20		5
11	20		5
12	24	+	5
13	24	+	5½
14	26		4
15	27		4
16	27		5
17	30		5
18	30		5½
19	30		5½
20	30		5½
21	30		5½

Case	Age, Months	Schick Test	Months After Last Rub
22	30	+	4
23	34		4
24	36	+	5½
25	36	+	5
26	36		5½
27†	36		5
	Years		
28	2½		6½
29	4		6½
30	4		4½
31	4	+	5
32	4½	+	7
33	5		5
34	5		6½
35	6½		5½
36	6½	+	4½
37	7		5½
38	7		5½
39	9		5
40	13	+	5½
41	13	+	5
42	13	—	5½

Positive cases	12
Negative cases	30
Total cases	42
Percentage negative	71.4

* Case 4 was positive after two and one-third months.
† Case 27 was slightly positive after three months.

TABLE 2.—*Control Schick Test Five Months After the Last Rub; Group II*

Case	Age, Years	Schick Test	Case	Age, Years	Schick Test
1	8	+	5	16	+
2	10	—	6	16	—
3	11	+	7	16	—
4	13	—	8	17	—

Positive cases	3
Negative cases	5
Total cases	8
Percentage negative	62.5

treatment. European experience with toxin-antitoxin mixture is well exemplified in the work of Seligmann.[12] After treating 11,325 children with toxin-antitoxin, he obtained 71 per cent negative control Schick tests, which is practically the same as the results that have been obtained by the percutaneous method.

Loewenstein claimed that the reported percentage of children reacting negatively to the Schick test after immunization by the percutaneous

12. Seligmann, E.: Deutsche med. Wchnschr. **55**:1117, 1929.

method would be higher were the control Schick tests made at a later period. This interesting point is illustrated by two of our cases in group 1. The first case is that of a child, aged 19 months, who showed a positive Schick test two and one-third months after the last rub, but who gave a negative reaction when tested five and one-half months afterward. The second case is that of a child, aged 3½ years, in whom the Schick test was positive after three months, but negative after six and one-half months. The longer period of time between the last rub and the control Schick test may also help to explain the 85 per cent of negative cases in group III, which was given control tests after six months, as compared with the negative 62.5 per cent in group II, which was given control tests after only five months.

In his last published communication, Loewenstein [13] stated that Baar obtained 81 per cent negative control Schick tests. He ascribed this

TABLE 3.—*Control Schick Test Six Months After the Last Rub; Group III*

Case	Age, Years	Schick Test	Case	Age, Years	Schick Test
1	6	+	7	13	−
2	7	−	8	14	−
3	10	−	9	14	−
4	12	−	10	14	−
5	13	−	11	14	+
6	13	−	12	15	+

Positive cases	3
Negative cases	9
Total cases	12
Percentage negative	85

increased percentage to an improvement in the preparation and in the technic of administration.

It is generally considered that a negative Schick test shows that a patient has about $\frac{1}{30}$ of a unit or more of diphtheria antitoxin in 1 cc. of blood serum. Many investigators, however, agree with Loewenstein, who stated the belief that a negative Schick test is given too great prognostic value and that such a result does not always mean complete immunity against diphtheria.

With this idea in mind, the Schick test would not be a sufficiently reliable index to determine the efficacy of any preparation used to induce an active immunity against diphtheria. For this purpose, the determination of the antitoxin content per unit of serum is more reliable. Such studies have been made by Baecher and Loewenstein [14] on children immunized by the percutaneous method. Their results showed that the toxoid ointment of Loewenstein definitely increases the antitoxin content of the blood serum, the quantity varying from $\frac{1}{20}$ to 1 unit per cubic centimeter of serum.

13. Loewenstein, E.: Munchen. med. Wchnschr. **77**:21 (May 23) 1930.

14. Baecher and Loewenstein: Ztschr. f. Immunitätsforsch. u. exper. Therap. **54**:21, 1927.

Table 4 indicates the antitoxin content per cubic centimeter of serum as determined by Baecher from a number of cases immunized by Loewy with Loewenstein's ointment.

It has been indicated that an increased incidence of diphtheria occurs during the first six weeks following the administration of toxin-antitoxin because of the so-called negative phase. Loewenstein stated that his ointment induces no negative phase, and accordingly an increased susceptibility to diphtheria from this cause is eliminated. His conclusions, however, are drawn from clinical studies on several thousand children who were immunized by his method, none of whom developed diphtheria during the first six week period. More recent studies by Basch,[15] who combined clinical observations with determinations of the antitoxin content of the serum, show that Loewenstein's ointment, similar to the antitoxin mixture, does produce a diminution of the antitoxin content of the serum, which begins from six to twelve days after treatment and may last from six to eighteen days.

In the reports on the several thousand children who were immunized against diphtheria by the percutaneous method, no investigator observed

TABLE 4.—*The Antitoxin Content of Blood Serum Produced by Loewenstein's Ointment*

Antitoxin content per cc. serum..	1/50	1/20	1/15	1/10	1/7	1/5	1/4	1/2	1
Number of cases.....	6	11	5	1	2	3	2	3	6

a single instance of a constitutional reaction. Loewy reported patients in whom there were slight elevations of temperature. In every case the children had tuberculous bronchial glands. In none of our patients did we observe any constitutional reactions.

In one third of her cases, Loewy reported that she saw a skin irritation over the field of inunction. The rash was characterized by small nodules and pustules of varying sizes and resembled in appearance the papulopustular rash produced by the tuberculin ointment of Loewenstein. We observed a similar eruption in a number of our cases. The rash usually appeared from about two to three days following the rub, was limited to the area of the skin that had been treated, and had either a papulovesicular or a papulopustular character. There were no subjective symptoms. The lesions disappeared after from seven to ten days without treatment.

CONCLUSIONS

1. The clinical experience and the immunologic studies with Loewenstein's percutaneous method of immunization against diphtheria are

15. Basch, F.: Beitraege zur aktiven Immunisierung gegen Diphtherie, Wien. klin. Wchnschr. **43**:449, 1930.

sufficiently satisfactory to justify its use. 2. It is a simple, practical and expedient method, which produces active immunity against diphtheria in as large a percentage of cases as is induced by other methods now in general use. 3. It avoids the dangers which may occur by introducing a foreign protein directly into the lymphatic circulation. 4. It eliminates the danger of liberating free toxin in the system. 5. It avoids the occurrence of constitutional reactions. 6. It does not sensitize the child to other serums.

If long tried clinical experience proves Loewenstein's percutaneous ointment to be an immunizing agent of definite value, its use will become the method of choice.

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SONNE DYSENTERY

A REPORT OF THIRTY CASES OF DYSENTERY IN CHILDREN CAUSED BY B. DYSENTERIAE SONNE *

RICHARD L. NELSON, M.D.

BOSTON

Sonne,[1] in 1915, while studying dysentery in Copenhagen, found the chief causative agent to be a late lactose-fermenting bacillus, closely resembling the Flexner bacillus, but serologically specific and different from it. Prior to his description of this organism, other workers had encountered similar bacilli in dysentery and diarrheal disease, but had failed to establish a true etiologic relationship.[2] Following Sonne's description, workers in France, Denmark, Norway, Sweden, Scotland, England, Australia and Japan [3] reported the finding of Sonne organisms in cases of dysentery. Others have reported the finding of similar organisms which may or may not be the same.[4] Despite the rather frequent finding of Sonne dysentery in many parts of the world, cases of this disease have seldom been reported in this country. Recently, Gilbert and Coleman [5] reported the occurrence of twelve cases

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* Since this paper was submitted for publication, eighteen additional cases of Sonne dysentery have been seen; six in infants under 2 years of age, in which group there was one fatal termination, and twelve in children over 2 years of age, with one fatality. One of these cases, that of a patient of Dr. Harlan F. Newton at the Peter Bent Brigham Hospital, was exceedingly interesting in that Sonne organisms were simultaneously isolated from the blood stream and the feces at the height of the fever. This case will be reported in detail by Dr. Newton.

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1. Sonne, C.: Ztschr. f. klin. Med. **81**:73, 1915.

2. Duval, C. W., and Schorer, E. H.: Bacteriological and Clinical Studies from the Rockefeller Institute for Medical Research, 1904. Duval, C. W.: Another Member of the Dysentery Group, J. A. M. A. **63**:381 (Aug. 6) 1904. Torrey, J. C.: J. Exper. Med. **7**:365 and 385, 1905.

3. D'Herelle, H.: Ann. de l'Inst. Pasteur **30**:145, 1916. Thjøtta, T.: J. Bact. **4**:355, 1919. Mita, K.: J. Infect. Dis. **29**:580, 1921. Wiseman, W. R.: J. Hyg. **26**:187, 1927. Patterson, S. W., and Williams, F. E.: J. Path. & Bact. **25**:393, 1922. Nabarro, D.: J. Path. & Bact. **26**:429, 1923; **30**:176, 1927. Bamforth, J.: J. Hyg. **22**:343, 1923. Smith, J.: J. Hyg. **23**:94, 1924. Fraser, A. M.; Kinlock, J. P., and Smith, J.: J. Hyg. **25**:453, 1926. Channon, H. A.: J. Path. & Bact. **29**:496, 1926. Fyfe, G. M.: J. Hyg. **26**:271, 1927.

4. Andrewes, F. W.: Lancet **1**:560, 1918. Castellani, A.: Am. J. Trop. Med. **7**:199, 1927; J. Trop. Med. **31**:185, 1928.

5. Gilbert, R., and Coleman, M. B.: Am. J. Pub. Health **19**:312, 1929.

of dysentery in New York state caused by the Sonne bacillus, four cases occurring in two state hospitals, five cases in a city during an epidemic of enteric disease attributed to a polluted water supply and the remaining three cases in widely separated counties. Castellani [6] has recovered late lactose-fermenting bacilli from cases of colitis and paratyphoid-like infection, to which he has given the name "metadysentery bacilli." These I have shown [7] to be identical with the Sonne bacillus.

Since the preparation of this paper Johnson and Brown,[8] in Toronto, have reported the isolation of twenty-one strains of *B. dysenteriae* Sonne.

During a period of seven months, thirty cases of dysentery in children [9] caused by the Sonne organism, have been seen. Some difficulty was experienced in the identification of the causative organism in the earlier cases, and it was for a time regarded as an atypical form of the Flexner bacillus. But with the development of more cases of the disease, immune rabbit serums were prepared and a culture of a known Sonne strain obtained from the American Type Culture Collection in Chicago, and culture comparisons and cross-agglutination reactions that established the true identity of the organism were carried out.

BACTERIOLOGY

All dysentery bacilli possess the common characteristics of being non-motile, gram-negative coliform bacilli, fermenting dextrose with the formation of acid, and not producing gas in any carbohydrate. They may be divided into two main groups: those failing to ferment mannite (Shiga, Shiga-Kruse) and those fermenting mannite. The former group contains only one organism and is but rarely seen in this country. The mannite-fermenting group contains a number of organisms, the most common being the Flexner bacilli, which may be serologically divided into a number of subgroups so as to include the Hiss bacillus, which was formerly separately classified on the basis of its failure to ferment maltose, a characteristic possessed by the other Flexner bacilli. The other members of the mannite-fermenting group are the Strong bacillus, characterized by the fermentation of saccharose, and the Sonne bacillus, characterized by the latent fermentation of lactose, which will be

6. Castellani (footnote 4, second and third references).

7. Nelson, R. L.: J. Bact. **20**:183, 1930.

8. Johnston, M. M., and Brown, Alan: Canad. Pub. Health J. **21**:394 (Aug.) 1930.

9. During this same period, three cases of Sonne dysentery were seen in adults, two in nurses and one in the wife of a physician.

described here. The Shiga, Strong, and Sonne bacilli are readily distinguishable from the Flexner bacilli and from each other by serologic methods.

Before describing the Sonne bacillus, it may be well to give briefly the method employed in this clinic for the isolation and identification of the various members of the typhoid-dysentery group of organisms. This is as follows:

As soon as possible, after passage, the stool specimen is brought to the laboratory, where it is plated on an eosin-methylene blue agar plate. After twenty-four hours' incubation, the plate is examined for suspicious colonies; if these are present, they are fished to Russell's double-sugar agar slants. Organisms giving a suspicious reaction on Russell's medium are then tested for motility; twenty-four hour broth cultures grown at room temperature, run through fermentation tests and later agglutinated with appropriate immune serums are used. For the routine fermentation tests, eight sugars are employed: dextrose, mannite, maltose, lactose, xylose, rhamnose, saccharose and dulcite. These sugars are incubated for at least four days in order to pick up any latent fermentation, which is so important in the identification of the Sonne bacillus.

B. dysenteriae Sonne has been found to differ but little from other dysentery bacilli. It is a short, coliform bacillus, showing a tendency toward involution forms. It is decolorized by Gram's method of staining. It does not liquefy gelatin, even after twenty-one days' cultivation on this medium. Indol is never produced. Litmus milk is rendered acid after twenty-four hours; but clotting does not occur even after twenty-four days, the milk remaining acid throughout this period.

On eosin-methylene blue agar plates, the Sonne bacillus produces round, well defined, grayish white to clear colonies, indistinguishable from the colonies of other dysentery bacilli after twenty-four hours' incubation. However, after longer cultivation, the colonies become larger, more irregular in outline, and present a more or less characteristic crenated border. On plain hormone agar and in liquid mediums the growth is not different from that of other members of the typhoid-dysentery group of organisms.

Some variation has been observed in the fermentation reactions of the organism, but this should not prove confusing, in that the variation has occurred in sugars not ordinarily employed in routine work. With the eight sugars employed as a routine, the reactions have been constant and distinctive. Dextrose, mannite, maltose and rhamnose are fermented with the formation of acid, but no gas, in twenty-four hours. The fermentation of rhamnose at once directs attention to the fact that the organism may be a Sonne bacillus, for only the rarer forms of Flexner

bacilli possess the property of fermenting rhamnose. Lactose is slowly acidified, three to six days usually being required for the change to become apparent, though in rare instances it may occur earlier. It is this latent lactose fermentation that distinguishes the Sonne bacillus from other organisms of the dysentery group. It is not improbable that many cases of Sonne dysentery are either not recognized bacteriologically or are wrongly classified as atypical Flexner dysentery, because the sugars are not incubated sufficiently long to pick up this latent lactose fermentation. Indol is never produced by this organism.

Serologically, the Sonne bacillus is easily differentiated from the other dysentery bacilli; and it is the agglutination reactions of the organism that serve as the final criteria for its identification. Immune serum, prepared by the intravenous injection of increasing doses of a formaldehyzed suspension of the organisms into rabbits, contains few if any agglutinins against other enteric bacilli; in this serum the Sonne bacillus is readily agglutinable, even when recently isolated cultures are employed. The immune serums prepared here have had an agglutinating titer of over 1 : 5,000.

CLINICAL FEATURES OF SONNE DYSENTERY

From August, 1929, to February, 1930, thirty cases of dysentery in children have been encountered in which the causative agent proved to be *B. dysenteriae* Sonne. The children varied in age from 15 months to 10½ years.

In general, it may be said that the Sonne dysentery bacillus produces a very mild form of enteric infection, with symptoms of short duration and mild intensity. Exceptions to this statement have been noted in practically all reports of any considerable number of cases. Fraser, Kinlock, and Smith,[10] in Aberdeen, studied thirty-three cases of this infection. They said:

> There is a notable variation in the degree of severity of the dysenteric symptoms in different cases of Sonne dysentery. In exceptional cases the symptoms are of an urgent description; and two varieties of these urgent forms can be recognized. In one variety the symptoms simulate those of an acute Flexner dysentery with sudden onset of illness, diarrhea and colic, and the rapid appearance of blood and mucus in the stools. In the second variety of the urgent form of the disease the symptoms simulate those of Salmonella infections, or the choleraic form of dysentery, with sudden onset, epigastric pain, vomiting, diarrhea with green stools containing mucus but no blood, and rapid prostration.

These authors found the majority of cases of the disease to be of much milder intensity, with an irregular, subacute diarrhea with green

10. Fraser, Kinlock and Smith (footnote 3, tenth reference).

stools containing mucus and a transient and commonly slight rise of temperature. They observed a catarrhal condition of the respiratory system in many of the cases, which varied from a simple catarrh of the upper respiratory passages to an acute bronchitis, and which occurred either coincident with the development of abdominal symptoms or preceded them. They believed this respiratory involvement to be a notable feature of the disease.

In the cases seen here, seven have been classified as of severe nature, the other twenty-three having been of mild character. In the severe cases, the onset was usually sudden, with loss of appetite, feverishness, irritability and drowsiness. Vomiting and convulsions occurred at the onset in a few cases. These symptoms were followed in from a few to twenty-four hours by the frequent passage of small, loose, watery, green stools, containing mucus but usually no blood. The fever, which usually preceded the diarrhea, often remained elevated for from two to five days at a height of 104 to 105 F. During the febrile period there was usually disinclination to take food, and the child was content to remain in bed. The stools, which at first contained mucus, only later usually showed streaks of fresh blood. The chief feature of the severe cases was the degree of prostration present, which in most of this group was marked. Unless the children were vigorously treated, the manifestations of dehydration and ketosis from the loss of fluids by bowel were apt to develop. After four or five days the temperature usually returned to normal, but the diarrhea often persisted for about a week, when the stools became normal in number, but were soft and unformed for some days more. In our severe cases, there was one death directly attributable to the dysenteric infection (case 2). This case, the report of which will be given in detail later, was interesting in that diarrhea was absent, and diagnosis could not be established until the postmortem examination revealed the typical lesions of bacillary dysentery. The other patients in this group recovered without complications.

In the milder and larger group of cases, the disease was usually ushered in by a sudden rise of temperature to from 102 to 104 F., anorexia and a feeling of lassitude. The prostration observed in the more severe cases was lacking. The febrile onset was followed in most cases in from twenty-four to forty-eight hours by diarrhea, four to ten loose, green, watery stools containing mucus being passed during the day. Blood was absent in most stools, but was usually present at one time or another in any individual case. The elevation of temperature was usually of short duration, from twenty-four to forty-eight hours, but in a few cases it persisted for longer periods. In those cases in which the fever persisted for longer than forty-eight hours, it was usually at a low level, and the child did not feel particularly sick. With

the subsidence of the fever, the children usually regained their appetites and otherwise felt well, though they continued to have an increased number of stools for about a week. In most cases, the diarrhea was never urgent; tenesmus and abdominal pain were not present. In this milder group of cases, there was one fatality, but the Sonne infection was superimposed on a cardiac decompensation and could be considered little more than a contributing cause of death. Unfortunately, autopsy was not permitted in this case.

Respiratory symptoms were lacking in most of the cases seen here. It is true that a slight mucus nasal discharge was present in a few cases, but not in enough cases to make us agree with Fraser, Kinlock and Smith,[10] in considering respiratory symptoms a notable feature of the disease. As noted, blood in the stools has not been a prominent feature in these cases, but we believe that careful examination of all stools passed will disclose its presence in nearly every case at one time or another. The amount of blood in the stools is of value in differentiating the Sonne from the Flexner type of dysentery, the stools in the latter disease often consisting of pure blood and mucus, while such stools are rare in the Sonne type.

The following case histories are introduced as illustrative of the more severe forms of the disease.

REPORT OF CASES

Case 1.—T. F., a white boy, aged 2 years and 11 months, was admitted to the hospital on Sept. 19, 1929, with the complaints of diarrhea and vomiting. He had been well until twenty-four hours before entry, when he vomited the lunch he had eaten half an hour previously. At that time he seemed drowsy and feverish, and soon passed a large, green, watery stool. He was put to bed. During the afternoon he passed eight loose stools, and vomited about six times. No blood or mucus was noted in the stools. That night he seemed quite weak and listless, and began to show twitchings of the extremities every few minutes, but he had no generalized convulsions. A physician was called, who advised hospitalization.

He was admitted to the hospital twenty-four hours after the onset of the disease. Examination showed a restless, irritable, acutely ill child. His face was flushed, and there was a temperature of 104 F. There was a thin, mucus, nasal discharge and slight tenderness in the right lower quadrant of the abdomen. Otherwise, the results of the examination were negative. In the hospital he passed daily four or five loose, green, watery stools, containing blood and mucus for several days. After the third day the blood disappeared, and his appetite returned; by the fifth day his temperature was normal.

Laboratory data showed a leukocyte count of 27,500 on admission, with 82 per cent of the cells polymorphonuclears. Two days later, the leukocyte count was 10,700. Stool cultures on the third, fourth and fifth days after entry showed large numbers of Sonne dysentery organisms. The patient's serum on the fifth day failed to agglutinate Sonne, Hiss or Flexner organisms.

Case 2.—M. M., a white girl, aged 3½ years, was admitted to the hospital on Oct. 25, 1929, because of persistent vomiting and prostration. The history revealed

that since 18 months of age until the previous spring, she had had attacks of vomiting at regular intervals; since that time she had been free from symptoms. Thirty hours before entry, she began vomiting, and she continued to display this symptom, together with feverishness and great prostration. Diarrhea had not been noticed by the parents.

Examination showed a well developed and well nourished child, with flushed cheeks, an apprehensive expression, and considerable evidence of dehydration. The breathing was rapid, shallow and irregular, and there was an acetone odor to the breath. The tonsils were moderately enlarged, and both ear drums were thought to be injected. She was thought to have an acute infection of the upper part of the respiratory tract, with profound ketosis, though the condition of the throat and ears did not seem sufficient to account for the extreme prostration and a temperature of 105 F. Examination of the urine showed a trace of acetone, but the results were otherwise negative. Both ear drums were incised, without benefit. Energetic treatment was instituted to combat the ketosis and dehydration, but the symptoms continued unabated. Three days after admission, the patient suddenly became comatose, and respirations ceased a few hours later.

Postmortem examination showed evidence of marked dehydration, a fatty liver and engorgement of the esophageal and gastric mucosae. There were numerous hemorrhagic areas in the ilium and jejunum and swollen mesenteric nodes, suggesting an enteric infection. Microscopic sections through these hemorrhagic areas showed partial loss of the mucosal surface, diphtheritic inflammation of the mucosa, fibrin deposit and polymorphonuclear cell infiltration.

On cultures taken at autopsy from both the intestinal scrapings and the right ureter large numbers of colonies of *B. dysenteriae* Sonne grew.

Case 3.—P. M., a white boy, aged 3½ years, was admitted to the hospital on Jan. 1, 1930, because of convulsions. The family history revealed that one week before the onset of the patient's illness, a sibling, aged 44 days, had died of an unknown cause, and that four days before entry, another sibling, aged 19 months, had recovered from an attack of vomiting and diarrhea. The patient had been well until the night before entry, when he vomited and diarrhea developed; he passed eight loose stools containing mucus. The morning of the day of admission, the diarrhea continued, and he had two generalized convulsions, each lasting about fifteen minutes.

Examination showed a well developed and nourished child appearing acutely ill. The temperature was 103 F. The throat was injected, and there was evidence of marked dehydration and ketosis. Otherwise the results of the examination were negative.

Intravenous injections of dextrose and subcutaneous injections of salt solution were given immediately, with rapid improvement. The next day the temperature had fallen to 100 F., and the patient seemed much brighter, though he continued to have diarrhea and a slightly elevated temperature for about a week, after which time he seemed perfectly well.

Laboratory data showed the leukocyte count to be 8,150 with 84 per cent polymorphonuclears. Cultures of the stools on the day of admission showed numerous colonies of *B. dysenteriae* Sonne. Cultures of the stools were persistently positive until February 10, six weeks after admission. On February 13, an attempt was made to grow dysentery organisms from aspirated bile, but without success. The patient's serum on February 15 failed to agglutinate a Flexner dysentery antigen, but agglutinated Sonne organisms in a dilution of 1:40.

Comment.—Case 3 is interesting in that the patient continued to have *B. dysenteriae* Sonne organisms in his stools for at least six weeks after the onset of the infection.

Case 4.—J. G., a white boy, aged 5½ years, was admitted to the hospital on March 7, 1930, with the complaint of pain in the abdomen. The family history and the personal history were irrelevant to his present condition. Four days before entry the patient vomited and complained of pains in the stomach when he awakened in the morning. During the day he had seven or eight loose, green, watery bowel movements. That day he vomited everything taken by mouth except ginger ale. His bowels continued to be loose, and he wanted nothing to eat. The abdominal pain disappeared the day following onset, but returned two days later. At that time his temperature was 102.6 F. The day before entry he continued to have abdominal pain, wanted nothing to eat, and had a temperature of 104 F.

On entry to the hospital examination showed a somewhat undernourished but well developed child lying quietly in bed, but from time to time complaining of pain in the abdomen. Examination showed the abdomen to be soft, except over McBurney's point, where there was moderate tenderness and slight spasm. Rectal examination revealed generalized tenderness, more marked on the right. Otherwise the results of the examination were negative. The leukocyte count was 10,500.

Enteric precautions were taken at once, and a stool was sent to the laboratory. The child was thought to have dysentery rather than appendicitis, in view of the diarrhea, the character of the stools and the generalized abdominal pain and tenderness. The day following entry, the pain and tenderness had entirely disappeared. A stool culture revealed *B. dysenteriae* Sonne. The patient continued to have a slight elevation of temperature for several days, but in the hospital passed only one or two stools daily, and was sent home well after six days.

Comment.—Case 4 illustrates the difficulty that may be experienced, especially with children, in differentiating dysentery and appendicitis.

Case 5.—J. M., a white boy, aged 4 years and 2 months, was undergoing treatment in the hospital for deformed ears. A plastic operation was performed on Jan. 30, 1930, with normal postoperative convalescence until February 20, when his temperature suddenly rose to 104 F.; he seemed drowsy and irritable and refused food. At this time, there was nothing to account for the fever, which continued with considerable prostration. Two days later diarrhea developed, from four to six loose, blood-streaked stools containing mucus, being passed daily. Stool cultures at this time yielded many colonies of *B. dysenteriae* Sonne. The temperature remained elevated for four days; then it returned to normal, and except for the persistence of loose stools for several days, the child seemed perfectly well.

Laboratory data showed positive stool cultures for *B. dysenteriae* Sonne on February 20, 24, 26 and 27, and negative cultures on March 1, 4 and 5. On February 27, the patient's serum agglutinated a Sonne antigen in a dilution of 1:160.

The temperature chart for case 5 is introduced as typical of the more severe form of the disease.

The following case histories are illustrative of the milder form of the disease, in which the prostration is much less marked than in the preceding group, and the symptoms are usually of short duration and mild intensity.

Case 6.—R. D., a white boy, aged 7 years and 8 months, was in the hospital for the correction of deformities resulting from a tumor of the spinal cord. A tendon transplant operation was performed on November 22. The day following the operation the temperature rose to 101 F. and the pulse rate to 120. The next day he passed four loose, watery, green stools containing mucus but no blood. There was no vomiting, abdominal pain or other symptoms, except a slight indisposition to take food. The temperature varied between 99 and 101 F.

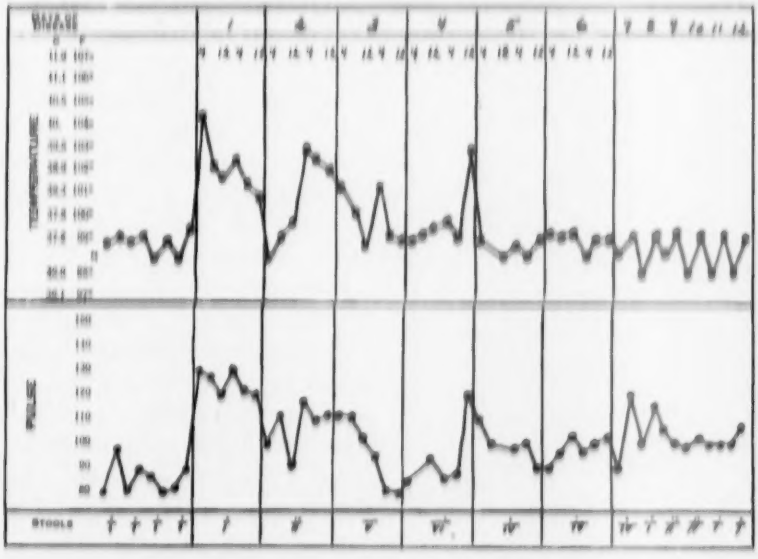

Chart 1 (case 5).—Temperature chart of a patient with the severe form of dysentery.

for the next six days, during which period he continued to pass from four to eight loose stools daily; otherwise he seemed well. After the sixth day, the temperature remained normal, and the stools became normal in number and character.

B. dysenteriae Sonne was isolated from a stool passed on November 28 and from the subsequent stools examined until December 7, when they became negative.

Case 7.—N. S., a white girl, aged 10½ years, was admitted to the hospital on Jan. 25, 1930, because of a probable rheumatic heart disease. In the hospital, she was without symptoms, except a temperature elevation from 99 to 101 F. On February 28, she showed a rise in temperature to 104 F., and a slight mucus nasal discharge developed. She passed several loose, but not particularly pathologic, stools on that date. During the next four days, she passed from three

to six loose stools daily, described as small, bloody and containing mucus. There was no vomiting, abdominal pain or other symptoms. The temperature fell to 101 F. the day after the onset, and thereafter remained at its former level until February 7, when she was discharged.

A stool culture on January 7 disclosed rare colonies of *B. dysenteriae* Sonne. All other cultures were negative.

Case 8.—S. L., a white girl, aged 6 years and 9 months, was operated on for streptococcus peritonitis on Dec. 28, 1929. Following operation, she had a temperature of from 103 to 105 F. for several days; then the temperature slowly subsided. By January 20, the operative wound was entirely healed, and she was

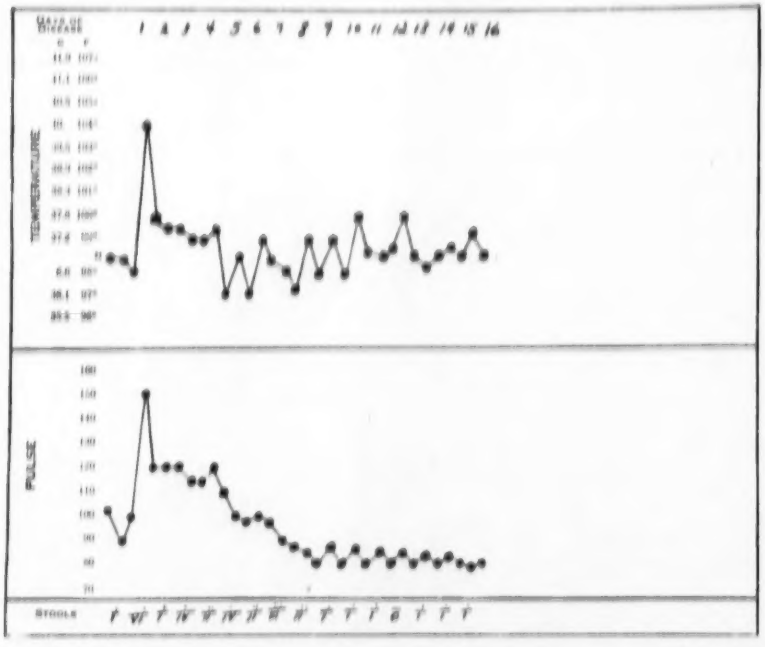

Chart 2 (case 8).—Temperature chart of patient with a mild form of dysentery.

doing nicely, though still showing an afternoon temperature of from 99 to 100 F. On January 27, the temperature suddenly rose to 104 F., and on the same day she passed six loose, green, watery stools containing blood and mucus. There were no other symptoms. The following day the temperature fell to its former level, and though she continued to pass from two to six loose stools daily for the next eight days, there were no other symptoms, and she felt well.

Stool cultures were positive for *B. dysenteriae* Sonne on January 30 and 31, and February 3. On February 7, the patient's serum agglutinated Sonne organisms in a dilution of 1:40.

The temperature chart from case 8 is introduced as typical of the majority of mild cases of Sonne dysentery.

COMMENT

The occurrence of thirty cases of dysentery in children in which *B. dysenteriae* Sonne was the causative agent would indicate that this organism may be important as a cause of dysentery in this country as well as in other parts of the world.

The rarity of reports of this disease in the American literature would make it seem important to draw attention to its bacteriologic and clinical features. This has been done in the preceding paragraphs.

There are several features of the disease that make it of especial importance:

The mildness of the majority of cases is apt to indicate that the causative organism is one of low virulence and consequently unimportant. That the organism is capable of assuming great invasive powers is shown in the pathologic observations in case 2.

The persistence of organisms in the stools of convalescents over long periods has been observed here in a number of cases, indicating that carriers are probably an important mode of transmission of the disease. Because of the mildness of the symptoms in many instances, especially in adults, children may readily be infected by elders who have suffered from a mild diarrhea.

Diagnosis is best established by the isolation of the Sonne organism from the stools. Agglutinins are present in the blood serum in many cases, but are often present in too low a titer to be of diagnostic value. A positive agglutination reaction with the serum diluted more than 1:80 is probably diagnostic. The absence of a positive agglutination reaction does not rule out a Sonne infection.

CONCLUSION

1. Attention is drawn to the possible importance of *B. dysenteriae* Sonne as a cause of dysentery in children.

2. Methods for the isolation and identification of the Sonne bacillus are given.

3. Clinical features of the disease with case histories and clinical charts illustrative of the mild and severe forms are given.

A SURVEY OF TUBERCULOSIS IN SCHOOLS IN COLORADO *

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At the suggestion of the Colorado Tuberculosis Association a survey of the cases of tuberculosis in the school was undertaken in the town of Aurora. The Fitzsimons Government Hospital, located at Aurora, ten miles from Denver, is the largest institution in the United States caring for patients with tuberculosis. It is not surprising, therefore, that a large proportion of the population, numbering 968, in the town consists of health seekers and tuberculosis "contacts." The economic status of most of the families is below that of families in the average American community. Crowded housing conditions and inadequate food budgets are common, and the incidence of juvenile tuberculosis here could be expected to be as high or higher than that in any community in the United States. The present study was designed to ascertain if this expected high incidence of juvenile tuberculosis actually exists, to determine also the relative incidence of tuberculous infection in native-born children and in those born elsewhere, and to discover the incidence among children having contact and among those not having contact with the disease, and the degree of activity of the infection in children reacting positively to the tuberculin test. It was also hoped that the study might demonstrate to the local and state authorities the need for open-air school rooms and for state care of indigent, incipient and active cases of tuberculosis in children.

The Colorado Tuberculosis Association financed the project and furnished the services of a Public Health nurse. A local committee efficiently assisted in the examinations, and the superintendent of schools carried on a most effective campaign of publicity and education, resulting in a degree of cooperation among the parents and the children which assured the success of the survey. Without such cooperation and the active interest and support of the local physicians, health surveys are of little value, and testing of the skin with tuberculin difficult, if not impossible

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Fortunately, also, we were not handicapped by the "tuberculophobia" which is endemic in most American communities. The residents of Colorado, and especially those of Aurora, take the presence of tuberculosis in their midst for granted, since this disease is responsible for many of them being in this state. The parents were willing and anxious to submit their children to a thorough physical examination, tuberculin tests and roentgen studies.

The public school has an attendance of 498. High school children over 15 years of age were examined but not included in this study; some of them refused examination. Most of the grade school pupils were included. Children were admitted by appointment, a careful personal and family history was obtained, height and weight measurements were taken and a search was made for physical defects. Two tuberculin tests were made on each child, the Mantoux method, using 0.1 mg. of diluted old tuberculin in 0.2 cc. of salt solution, being applied to one forearm, and the Craig test, or multiple puncture technic, to the other arm. The latter method and a comparison with other diagnostic tuberculin tests are reported elsewhere.[1] Reactions to the tests were read in forty-eight hours, and the children giving positive reactions were given an appointment for roentgen study at the National Jewish Sanatorium. Of the total enrolment, 311 children, or 62.4 per cent, consented to the terms of the examination. A much higher percentage would have been examined if all of the high school students had cooperated. A few preschool children under 4 years of age and high school students over 15 years of age were excluded from the analysis, which consists of the records of 283 children, aged from 4 to 15 years (table 1).

RESULTS OF THE SURVEY

The tuberculin tests gave positive results in 103 children, or 36.4 per cent of the whole group, increasing, as would be expected, from 17.4 per cent in the group aged from 4 to 7 years to 43.5 per cent in the group aged from 8 to 11 years and 49.2 per cent in that aged from 12 to 15 years.

Results of the two tuberculin reactions were practically always identical, although the Mantoux reaction was invariably larger than the Craig test. Measurement of the tuberculin tests included either the area of papulation or the area of erythema. Dickey[2] measured the

1. Forbes, R. P., and Steinburg, C. L.: Diagnostic Tuberculin Reactions, Am. J. Dis. Child. **40**:1230 (Dec.) 1930.

2. Dickey, L. B.: The Size of the Reacting Area in Intracutaneous Tuberculin Tests in Relation to Classification of Disease and to Other Clinical Factors, Am. J. Dis. Child. **38**:1155 (Dec.) 1929.

area of erythema and found this to increase in positive reaction with the age of the child. He also noted an increase in the size of the reaction in children having contact as compared with those not having contact with tuberculosis. In the present study the diameter of the papule, rather than the total area of erythema, was measured. Table 2 shows

TABLE 1.—*Summary of Results*

Number of children included in the study	285
Percentage of school population consenting to terms of the study	62.4
Percentage of all children reacting positively to tuberculin	30.4
Percentage of children reacting positively classified as having childhood tuberculosis	18.4
Percentage of whole group classified as having childhood tuberculosis	6.7
Percentage of children reacting positively classified as suspected of having childhood tuberculosis	18.0
Percentage of whole group born in Colorado	46.3
Percentage of children reacting positively born in Colorado	27.7
Percentage of children classified as having childhood tuberculosis born in Colorado	21.0
Percentage of children classified as having childhood tuberculosis born elsewhere	79.0
Percentage of whole group having a history of contact with tuberculosis	36.4
Percentage of children classified as having active childhood tuberculosis having had contact in the family with the disease	22.2
Percentage of children having no contacts classified as having active tuberculosis	13.0
Percentage of children reacting negatively having a history of contact with tuberculosis	29.4
Percentage of children reacting positively having a history of contact with tuberculosis	48.5
Percentage of children classified as having childhood tuberculosis having a contact with tuberculosis	68.4
Percentage of children reacting positively having contact with a tuberculous father	64.8
Percentage of children reacting positively having contact with a tuberculous mother	12.6
Percentage of whole group giving history of symptoms of fatigue	32.8
Percentage of children reacting negatively giving a history of symptoms of fatigue	38.3
Percentage of children reacting positively giving a history of symptoms of fatigue	23.3
Percentage of children classified as having childhood tuberculosis giving history of symptoms of fatigue	36.8
Percentage of whole group, from normal to 6% underweight	29.6
Percentage of children reacting negatively from normal to 6% underweight	30.0
Percentage of children reacting positively from normal to 6% underweight	30.0
Percentage of whole group from 8 to 15% underweight	31.9
Percentage of children reacting negatively from 8 to 15% underweight	31.0
Percentage of children reacting positively from 8 to 15% underweight	31.0
Percentage of whole group 15% or more underweight	5.1
Percentage of children reacting negatively 15% or more underweight	3.0
Percentage of children reacting positively 15% or more underweight	1.9
Percentage of whole group overweight	34.2
Percentage of children reacting negatively overweight	32.8
Percentage of children reacting positively overweight	36.9
Percentage of children reacting negatively presenting râles (bronchitis)	6.1
Percentage of children reacting positively presenting râles (bronchitis)	1.9
Percentage of children reacting negatively with history of frequent colds	34.0
Percentage of children reacting positively with history of frequent colds	25.0
Percentage of children reacting negatively with history of cough	12.8
Percentage of children reacting positively with history of cough	7.6

that children with a history of contact with the disease react with a slightly larger papule from the Mantoux method than children having no contact, and that the size of the reaction tends to be slightly greater in the groups of an older age, confirming Dickey's observations. However, with the Craig test very little variation in the size of the papule was noted in relation to either age or history of contact with tuberculosis.

The comparison of these results with other reported series of either selected or unselected cases has a limited value. The rate of morbidity and mortality of tuberculosis has declined rapidly and consistently during the past thirty years, so that surveys made from ten to fifteen years ago are obviously not comparable with conditions in 1930. Thus, Friedman,[3] in 1919, reporting on von Pirquet tests in 464 Colorado children, found reactions to be 13 per cent positive in children from 5 to 6 years of age and 55 per cent in children from 10 to 14 years of age, and an average incidence of 39.4 per cent in the whole group, which included children from birth to 18 years. We are certain that these high figures would not be found today. We [1] recently tested all of the children in the Denver Orphans' Home,[2] using the same technic as in the present study, and found that only 20 per cent reacted positively in spite of the fact that many of the children came from homes broken up by tuberculosis. The incidence of positive reactions to tuberculin in

TABLE 2.—*Size of Reactions* *

Age of children		4-7 years	8-11 years	12-15 years		Average
Mantoux method	Contacts	7.7	9.2	8.6	or	8.6
	Noncontacts	8.3	6.4	7.8	or	7.5
Craig method	Contacts	4.1	5.0	4.9	or	4.7
	Noncontacts	4.3	3.9	4.9	or	4.6

* The figures indicate the diameter of the papules (not the erythema) in millimeters.

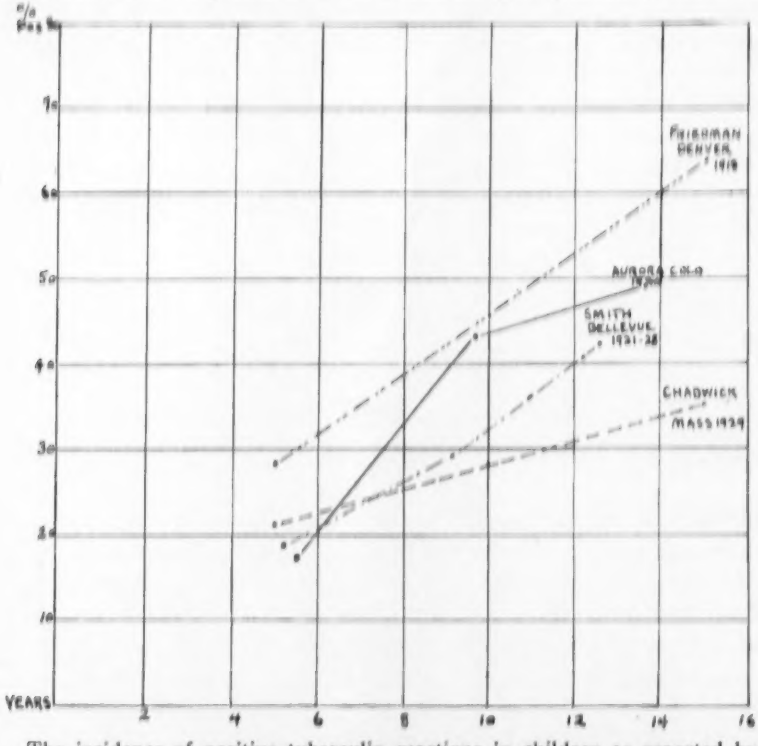
the children of Denver would doubtless prove to be less than that of an orphanage group. Chadwick's [4] observations on 42,071 children in Massachusetts may be taken as a norm, at least for the eastern states in 1929. He found 21 per cent positive reactions in children 5 years of age, 28 per cent in those 10 years of age and 35 per cent in those 15 years of age, the average for the whole group being 28 per cent. Since the death rate from tuberculosis in Massachusetts has declined from 144 in 1917 to 73 per 100,000 in 1927, the incidence of infection must also have declined rapidly.

The present study may be said to concern a selected group since less than half (46.3 per cent) of the children were born in Colorado, and since such a high percentage (36.4 per cent) gave a history of contact with tuberculosis in the family. Of the nineteen patients classified as having childhood tuberculosis in this series, only four, or 21 per cent, were born in Colorado, and only 27.3 per cent of those giving positive

3. Friedman, E.: Von Pirquet Test and Results of Its Use in 464 Colorado Children, Colorado Med. **16**:246 (Oct.) 1919.

4. Chadwick, H. D., and Zacks, D.: The Incidence of Tuberculous Infection in School Children, New England J. Med. **200**:332 (Feb. 14) 1929.

reactions to tuberculin were born in this state. Although 6.7 per cent of the children in this study were classified as having childhood tuberculosis, this figure does not compare unfavorably with the 1 to 4 per cent estimated for the average American community, when one considers that over a third of these children were in intimate contact with the disease. In fact, it is rather amazing that both the number of children giving positive reactions (36.4 per cent) and the number of those classified as having childhood tuberculosis (6.7 per cent) were not at



The incidence of positive tuberculin reactions in children as reported by previous investigators. The curve of Chadwick might be considered as a norm for the eastern states in 1929. Both the Aurora 1930 and the Denver 1918 curves are doubtless much higher than the average for either Denver or Colorado in 1930.

least double these figures. The deduction seems justified that climatic factors, such as altitude, low humidity and a high percentage of days with winter sunshine, act as prophylactic as well as therapeutic agents. Chadwick [4] noted that the incidence of tuberculous infection was twice as great in children having contact with tuberculosis, and Friedman [5] found two and one-half times as many positive reactions to tuberculin among such children. In the present study, 48.5 per cent of those

reacting positively, and 29.4 per cent of those reacting negatively gave a history of family contact with tuberculosis. That intimate and prolonged family contact is responsible for massive infection and the production of childhood tuberculosis is evidenced by the fact that thirteen, or 68.4 per cent, of the nineteen patients classified as having had childhood tuberculosis gave a history of family contact with the disease. The mother was reported to be tuberculous in only thirteen cases, but the father was tuberculous in sixty-six instances, or in 64.8 per cent of all the histories of contact with the disease.

Symptoms of fatigue, either nervous or physical, are generally quoted as being of particular significance in the diagnosis of juvenile tuberculosis. Reference to the accompanying chart shows that in this series, at least, a history of symptoms of fatigue was of no value in differentiating either the group reacting positively to tuberculin or that having childhood tuberculosis from the uninfected group.

Similarly, undernutrition apparently has no relation to childhood tuberculosis for children giving both positive and negative reactions showed almost identical percentages (Baldwin-Wood tables were used); in fact, there were fewer seriously underweight children (15+ per cent) among those reacting positively (1.9 per cent) than among those reacting negatively (3.9 per cent). Overweight was noted more frequently among the children reacting positively. Blatt,[5] Friedman,[5] Green and one of us (R. P. F.)[6] and others previously noted this dissociation between tuberculous infection in childhood and the state of nutrition.

Parenchymal lung signs, an indication of the adult type of tuberculosis, were not noted in any case, although a few children with mild cases of bronchitis were encountered. It so happened that most of the children showing râles gave negative reactions. Likewise, a history of frequent colds and of coughs was elicited more frequently from the children reacting negatively than from the infected group.

CONCLUSIONS

1. The statistics for the mortality and morbidity of tuberculosis in children today and ten years ago are not comparable.

2. The number and the size of positive reactions increase in children commensurate with contact and age, as noted by Dickey.

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5. Blatt, M. L., and Greengard, J.: Pericarditis as a Primary Clinical Manifestation of Tuberculosis in Childhood, Am. J. Dis. Child. **35**:631 (April) 1928.

6. Green, B., and Forbes, R. P.: A Comparison of the Value of the Cutaneous and Intracutaneous Tuberculin Reactions, Arch. Pediat. **43**:736 (Nov.) 1926.

3. The incidence of tuberculous infection among children varies greatly in different parts of the country, and is influenced by climatic and other environmental factors.

4. A survey for tuberculosis in the school of a small community composed largely of health seekers, when contact with the disease is unusually great, showed 36.4 per cent of 283 children from 4 to 15 years of age to be infected. This is only a moderate increase over the incidence noted in nontuberculous communities.

5. Roentgen studies of the 103 children giving positive reactions revealed childhood tuberculosis in 19 or 6.7 per cent of the whole group, the average for the country at large varying from 1 to 4 per cent.

6. No child with the adult or exudative type of tuberculosis was found.

7. Most of the children reacting positively and those having actual childhood tuberculosis were not born in Colorado.

8. Climatic factors in Colorado apparently exert a favorable influence in the protection of children against active tuberculous infection.

9. In this study, the father was the source of infection in 64.8 per cent of the children giving positive reactions, and the mother in only 12.6 per cent.

10. Symptoms of fatigue, undernutrition and a history of frequent colds are not reliable aids in the diagnosis of childhood tuberculosis.

AN INEXPENSIVE INCUBATOR FOR PREMATURE INFANTS*

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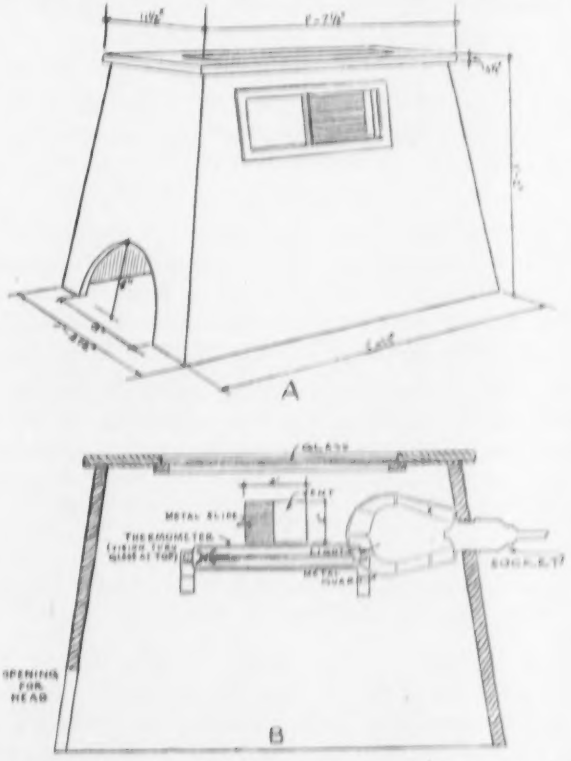
The problem of the regulation of body heat in the care of premature infants is ever present. Numerous devices have been in use, some complicated and expensive and others simple and less expensive. In nearly all there are mechanical features such as thermostats and ventilating



A, incubator for premature infants; *B*, longitudinal section of incubator.

devices which may, and often do, get out of order. The incubator here described is a copy, with a few minor variations, of one devised by Prof. E. Nobel of Vienna and used in the Children's Hospital of the University of Vienna.

It is made of well seasoned half-inch wood, preferably light wood. The joints should be dovetailed to make it more substantial, but they can be mortised if preferred. An arch, 4 inches (10 cm.) high by 8

* Submitted for publication, Aug. 1, 1930.

inches (20 cm.) wide, is cut in one end to permit the infant's head to lie outside the box. Heat is furnished by a 40 watt carbon film incandescent lamp at the opposite end from the arch. This lamp should be equipped with a metal wire guard to prevent blankets or clothing from coming in contact with the lamp bulb. An ordinary room thermometer is attached to one side wall with wooden or metal braces in such a manner as to be easily visible through the window in the top of the box. A vent measuring 3 by 2 inches (7.6 by 5.1 cm.), is made in each side wall just above the level of the thermometer; this is opened or closed by means of a metal slide to lower or raise the temperature. After experience in the use of an individual incubator box the temperature can be kept at almost any point between 90 and 110 F. as desired.

The incubator box is placed on an ordinary crib or bed mattress. The infant lies on the mattress with its head protruding from the arched opening. The infant's body is naked except for a gauze diaper. If the mattress is not flat and even, a rolled-up blanket may be placed around the bottom of the box to prevent cool air from entering.

These incubators have been used exclusively in the Presbyterian Hospital of Chicago for the past five years. Any good carpenter or cabinetmaker can make them at a slight expense. They have no mechanical devices which can get out of order. They are simple to manage and yet do not relieve the nurse of the responsibility of watching. (Any apparatus that takes away personal responsibility in the care of premature infants is bound to fail.) The infant breathes the atmosphere of the room and can be fed without being taken out of its warm enclosure.

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CELL AND PLASMA CHLORIDE IN THE PYLORIC STENOSIS OF INFANTS*

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In the pyloric stenosis of infants, quantitative changes are frequently found in the chemical constituents of the plasma. Thus, the alkali reserve may be increased, while the chloride content is often lowered (Hartmann and Smyth,[1] Maizels, McArthur and Payne [2]). The object of the following investigations was to determine whether similar changes occurred in the cell chloride, and whether such changes were relatively more or less marked.

METHOD

The foot is warmed if necessary, and blood is obtained by puncture of the great toe. The flow is usually fairly free, and the capillary blood, as a rule, is well oxygenated. The p_H of a sample of blood is determined by Martin and Lepper's method,[3] and the rest is allowed to flow under liquid paraffin in a small tube of the type described by Martin and Lepper.[4] Heparin is used to prevent clotting. The blood is centrifugated for half an hour at 3,000 revolutions per minute, and the bicarbonate and chloride content of the supernatant plasma is estimated by Payne's modification of Cullen and Van Slyke's method [2] and by Claudius' method,[5] respectively. The p_H of the residual plasma is then determined and the remnant of plasma and upper layer of red cells are carefully removed with a capillary pipet and teat, after which the chloride content of the red cells is estimated directly.

The hemoglobin of the blood is measured with Haldane's hemoglobinometer, and the hematocrit reading, by centrifugation of the blood in sealed graduated capillaries for half an hour at 3,000 revolutions per minute.

There are several possible sources of error inherent in the methods employed, as cell and plasma chloride, and hence the ratio of these two, depend on a number of factors, which may cause fairly extensive

* Submitted for publication, June 30, 1930.

* From the Department of Pathology, the Infants Hospital.

† Miss McArthur held the Robert Mond Research Studentship while engaged in this work.

1. Hartmann, A. F., and Smyth, F. S.: Chemical Changes in the Body Occurring as the Result of Vomiting, Am. J. Dis. Child. **32**:1 (July) 1926.

2. Maizels, M.; McArthur, C. B., and Payne, W. W.: Lancet **1**:286, 1930.

3. Martin, C. J., and Lepper, E. H.: Biochem. J. **20**:37, 1926.

4. Martin, C. J., and Lepper, E. H.: Biochem. J. **19**:573, 1925.

5. Claudius, M.: Acta med. Scandinav. **61**:4, 1924.

variations. The ratio of chloride per unit volume of cell to chloride per unit volume of plasma is represented by "R."

Two important factors that may cause variations in R are the degree of oxygenation of the blood and the reaction of the blood. R in venous blood is about 5 per cent higher than that in arterial blood;[6] as a rule, the blood collected in the present experiments is bright red, and is presumably well oxygenated. Therefore, variations in R due to imperfect oxygenation are likely to be considerably less than 5 per cent.

The effect of the reaction of the blood is more important, for R decreases rapidly as the p_H of the blood increases.[6] The p_H of a specimen of blood collected in a vessel depends on the reaction of the blood in the body; but this is always modified by the loss of carbon dioxide during the process of collection, as the blood flows down the side of the tube. This loss of carbon dioxide raises the p_H and so decreases the value of R. In earlier investigations, insufficient attention was paid to this effect of the p_H on R, but later, the p_H of the plasma separated from collected blood was determined. When this value is known, it is indicated in column 6 of the accompanying table.

In any case, the p_H of the blood hardly ever shifts more than 0.15 during collection, and rarely more than 0.1, changes that correspond to a decrease of R by —9 and —6 per cent, respectively.

In addition to the aforementioned sources of variation, R might appear to be altered by the presence of residual plasma between the centrifugated red cells, raising the apparent cell chloride, or by chloride in the added anticoagulant raising the content of the plasma, or through errors in the measurement of the material or reagents.

The apparent chloride content of the red cells increases with the amount of residual plasma in the cell masses. This residual plasma tends to be greater in tubes with wider bores. To test if this source of error were significant, blood was centrifugated for thirty minutes at 3,000 revolutions per minute, in a tube with a bore of 5 mm., and for one hour in tubes with a bore of 2 and 1 mm. The chloride content of each tube was determined. The results were in good agreement, and the divergence was not greater than could be accounted for by errors in measurement alone.

Heparin, in the quantities used, does not contain sufficient chloride to affect the results appreciably.

Duplicate estimations of chloride in 0.05 cc. of material have shown that the maximum probable error for plasma is ± 1.5 per cent, and for red cells, ± 5 per cent. Such variations could not decrease the value of R by more than 6.5 per cent. Therefore, the maximum decrease of R,

6. Henderson, L. J.: Blood: A Study in General Physiology, New Haven, Conn., Yale University Press, 1928.

by all these factors, is not likely to exceed 12.5 per cent, nor the increase of R to be greater than 6.5 per cent, unless the blood were very venous, when R might increase by a total of 11.5 per cent.

In all investigations, the methods of collection and centrifugation were standardized so far as possible, and in twenty-five normal infants under 3 months of age, R always lay between 0.44 and 0.56. In nineteen of these, R was between 0.47 and 0.53. Hence, notwithstanding all possible sources of error, in normal infants, the range of R is fairly narrow.

RESULTS

Normal infants under 3 months of age (twenty-five observations) showed: from 22 to 28 millimols of plasma bicarbonate, from 96 to 106 millimols of plasma chloride and from 44 to 56 millomols of cell chloride. R was estimated to range from 0.44 to 0.56. The highest shift of p_H observed after collection was 0.14; the mean was 0.07. In only one of the eight observations was the shift above 0.1 p_H.

Infants with Pyloric Stenosis.—Thirty-three infants with vomiting and marked gastric delay, as shown by roentgenograms, were examined. The records of twenty-six of those who had received the fullest investigation are shown in the accompanying table. The cases are arranged in order of their bicarbonate values. In cases examined before treatment has been commenced, the plasma bicarbonate may be normal or it may be increased to a considerable extent.

The p_H of the blood is usually increased in a corresponding manner, but not to the extent that might have been anticipated from the bicarbonate level. This compensation is probably brought about by underbreathing and the retention of carbon dioxide.

The plasma chloride may be normal; often, however, it is notably diminished (cases 5, 9, 14, 15, 17, 18, 19, 20, 21, 22, 23, 24, 25 and 26). The amount of plasma chloride is usually low in the cases in which the alkali reserve is raised.

At the outset, before treatment, R may be normal, but is usually decreased (in twenty-two of thirty-three observations). In other words, even when the amount of plasma chloride is low, the reduction of cell chloride may be still more extreme. The value of R cannot be correlated with the reaction of the blood (as shown directly by the p_H estimation, or indicated indirectly by the alkali reserve). It cannot be correlated with the chloride content of the plasma, or with the sum of bicarbonate and chloride molarities. It bore no apparent relation to the hemoglobin of the blood, to the relative cell volume or to the ratio of these two.

As the hemoglobin during the second month of life is usually below 90 per cent, and often below 80 per cent, the hemoglobin of the blood in pyloric stenosis often appeared to be increased (cases 1, 3, 4, 6, 7, 8, 13,

Results of Investigations in Twenty-Six Cases

Case	Age, Weeks	Weight, Pounds	Duration of History	Date	p_H of Blood	p_H of Separated Plasma	Plasma Bicarbonate, Millimols	Plasma Chloride, Millimols	Cell Chloride, Millimols	HCO_3 + Cl Plasma (Millimols)	R $\left(\frac{\text{Cell Chloride}}{\text{Plasma Chloride}}\right)$	R Calculated at p_H 7.40	Hematocrit Reading per Cent	Hemoglobin, per Cent	Comment
1	6	7¼	10 days	3/17/30	....	7.43	24.0	96	35	120	0.36	0.37	59.0	103.0	No operation
				3/20/30	7.34	7.41	22.1	102	42	124	0.42	0.42	50.5	81.0	
				3/24/30	....	....	19.2	112	54	131	0.48	....	....	100.0	
2	5	7	6 days	2/21/29	7.40	....	24.4	97	55	121	0.57				
				2/25/29	7.35	....	22.4	98	58	120	0.59				
3	6	4	6 weeks	5/13/30	7.40	7.50	26.6	99	37	126	0.37	0.39	46.7	105.0	
4	3	6¼	7 days	2/ 5/30	7.41	....	27.4	86	41	113	0.48	....	57.0	97.0	No operation yet
				2/ 7/30	7.36	....	27.0	107	47	134	0.44	....	55.5	105.0	
5	5	8¼	7 days	1/11/29	7.33	....	27.4	79	34	106	0.43	....	....	....	Removed
				1/12/29	7.41	....	34.6	77	35	112	0.46				
				1/14/29	Operation										
				1/22/29	7.37	....	24.4	105	42	129	0.40				
6	5	7¾	5 days	2/15/30	7.34	....	28.2	97	37	125	0.38	....	59.0	101.0	Removed
				2/17/30	....	....	28.0	97	51	125	0.53	....	52.0	92.0	
				2/18/30	Operation										
				2/24/30	....	7.42	32.0	105	32	137	0.30	0.31	45.2	74.0	
				2/28/30	....	....	31.2	110	31	141	0.46	....	43.4	77.0	
				3/ 3/30	7.35	7.45	26.4	100	47	126	0.47	0.49	41.0		
7	5	6½	3 weeks	4/15/30	7.42	7.50	29.6	98	40	128	0.41	0.43	49.5	97.0	Removed
				4/17/30	7.41	7.45	23.0	95	41	118	0.43	0.44	51.5	98.0	
				4/23/30	....	7.42	24.0	96	38	120	0.40	0.40	46.0	86.0	
				4/29/30	7.39	7.42	28.2	94	40	122	0.42	0.43			
8	6	7	10 days	4/ 9/30	7.40	7.42	30.0	99	40	129	0.40	0.41	58.0	116.0	Removed
				4/12/30	7.39	7.43	30.7	93	50	124	0.54	0.55	52.0	107.0	
				4/14/30	Operation										
				4/27/30	....	7.41	24.2	99	45	123	0.45	0.46	47.5	85.0	
9	4	7¾	24 days	7/26/29	....	....	30.5	77	27	107	0.35	....	40.0	67.0	
				7/29/29	7.53	....	39.5	96	39	135	0.41				
				7/30/29	Operation										
				8/ 4/29	....	....	34.0	98	43	132	0.44	....	40.7		
10	6	5½	10 days	3/ 4/30	7.49	7.57	34.0	101	49	135	0.49	0.53	43.0	74.0	Removed
				3/ 5/30	Operation										
				3/11/30	7.40	7.53	17.2	100	51	117	0.51	0.55	50.0	67.0	
				3/18/30	7.37	7.42	23.8	88	45	112	0.51	0.52	40.5	86.0	
				3/20/30	....	7.47	22.0	108	52	130	0.49	0.51	40.5	72.0	
11	8	4½	3 weeks	2/18/30	....	....	34.7	108	48	143	0.44	....	26.8	48.0	Died
				2/20/30	....	....	34.3	110	36	144	0.33	....	20.4	43.0	
12	4	7¼	2 days	8/16/29	7.40	....	35.2	89	37	124	0.41	....	48.6	69.0	Removed
				8/19/29	Operation										
				8/29/29	....	....	30.3	104	47	134	0.45	....	37.0	60.0	

				8/19/29	Operation											
				5/29/29	....	....	30.3	104	47	134	0.45	....	37.0	96.0		
13	8	7¾	7 days	2/28/30	....	7.51	35.7	94	41	130	0.44	0.47	53.0	118.0		
				3/ 3/30	....	7.42	28.2	105	47	133	0.45	0.45	44.2	90.0		
				3/ 5/30	7.41	7.52	29.0	98	45	127	0.46	0.49	47.0	79.0		
				3/ 8/30	7.48	....	35.2	91	40	126	0.44	....	52.0	98.0	Still vomiting	
				3/ 9/30	Operation											
14	6	....	————	12/ 5/29	....	....	37.1	80	40	117	0.50	....	54.5	90.0	Recovered	
				12/ 6/29	Operation											
				12/13/29	7.40	....	33.3	99	45	132	0.46	....	44.3	91.0		
				12/18/29	7.36	....	26.5	106	46	132	0.43	....	44.5	81.0		
15	8	6¼	7 weeks	11/20/29	....	....	37.2	81	40	118	0.49	....	39.4	82.0	No operation	
				11/28/29	....	....	24.1	107	54	131	0.50	....	34.3	68.0		
16	5	6¼	10 days	6/ 4/29	....	....	39.2	90	39	129	0.33	....	44.3	.....	No operation; recovered	
				6/ 6/29	....	....	33.9	79	32	113	0.40	....	47.2			
				6/21/29	....	....	22.8	107	49	139	0.46	....	38.5	76.0		
17	4	6¼	10 days	4/ 5/29	....	....	40.8	82	31	123	0.28	....	.....	.....	Recovering	
				4/ 8/29	Operation											
				4/ 8/29	7.42	....	45.8	71	31	117	0.44					
				4/16/29	....	....	31.7	82	39	114	0.48					
18	10	6¾	3 weeks	4/28/30	7.53	7.62	41.5	76	39	117	0.39	0.44	36.3	67.0	No operation; recovered	
				4/30/30	7.43	7.52	25.2	93	32	118	0.34	0.37	35.2	69.0		
				5/ 2/30	7.41	7.47	30.4	96	36	126	0.37	0.39	32.7	66.0		
				5/12/30	....	7.48	20.3	101	50	121	0.50	0.52	37.5	72.0		
19	14	9	3 weeks	7/ 6/29	....	....	42.7	78	33	121	0.42	....	37.0	.....	No operation; recovered	
				7/ 9/29	7.53	....	42.5	77	35	119	0.45	....	33.0			
				7/15/29	....	....	35.7	82	36	118	0.46	....	36.0			
				7/23/29	7.41	....	31.7	101	46	133	0.46	....	33.3	58.0		
				7/27/29	....	....	21.6	98	48	120	0.49	....	28.7	54.0		
20	7	6¾	7 weeks	5/24/29	....	....	43.3	67	28	110	0.42	....	38.7	.....	Recovered	
				5/27/29	Operation											
				5/27/29	7.46	....	44.9	85	31	130	0.36	....	32.8			
				5/31/29	....	....	37.6	83	35	121	0.42					
21	4	9	2 weeks	5/ 5/30	7.49	7.55	44.4	80	28	124	0.35	0.38	42.5	85.0	No operation; recovered	
				5/ 7/30	7.55	7.58	45.5	70	29	115	0.41	0.46	43.0	77.0		
				5/ 9/30	7.55	7.58	39.2	87	32	126	0.37	0.41	38.0	72.0		
				5/20/30	7.40	7.49	30.1	95	41	125	0.42	0.45	41.5	77.0		
22	5	7	10 days	12/10/29	....	....	47.0	69	30	116	0.43	....	61.0	.....	No operation	
				12/12/29	....	....	45.2	86	36	122	0.42	....	60.0	107.0		
				12/16/29	....	....	35.0	93	47	128	0.51	....	58.0	104.0		
				12/23/29	7.42	....	34.0	85	42	117	0.51	....	64.0	110.0	Still vomiting	
23	9	8½	2 weeks	9/ 9/29	7.52	....	47.8	64	24	112	0.37	....	....	69.0	Recovered	
24	7	6	14 days	5/23/29	....	....	55.4	54	21	109	0.39	....	50.0	.....	Recovered	
				5/25/29	Operation											
				5/25/29	7.46	....	43.7	78	33	142	0.42	....	40.0			
				5/28/29	7.47	....	34.3	93	37	147	0.40	....	38.0			
25	4	9¾	16 days	8/22/29	....	....	57.0	77	33	134	0.43	....	51.0	97.0	Recovered	
				8/26/29	Operation											
				8/26/29	....	....	44.4	95	46	139	0.48	....	44.0	72.0		
				9/ 5/29	....	....	23.8	109	49	133	0.45	....	35.7	64.5		
26	5	5½	5 weeks	12/17/29	7.55	....	57.0	68	34	125	0.35	....	43.0	85.0	No operation; recovered	
				12/20/29	7.48	....	40.1	93	36	133	0.39	....	44.5	85.0		
				12/24/29	....	....	31.8	98	36	130	0.28	....	39.0	61.0		
				1/ 1/30	7.40	....	26.1	99	40	125	0.40	....	39.2	76.5		

14, 22 and 25). This is probably the result of dehydration caused by copious vomiting.

The relative cell volume is often increased. The hematocrit reading was over 50 per cent in seven of twenty-two observations. This is definitely above the normal figure observed during the second and third months of life (from 34 to 48 per cent in ten normal cases in this series, and from 30 to 40 per cent in seventeen of Bakwin and Rivkin's eighteen cases [7]). The apparent effects of the subcutaneous administration of physiologic solution of sodium chloride over a period of two days can be inferred from a comparison of the first and second examination of each case; they are as follows: Eleven of twenty observations showed from slight to moderate decrease of the plasma bicarbonate; fifteen of twenty observations, including cases 1, 2, 5, 6, 7, 8, 9, 16, 17, 19, 21, 24, 25 and 26, showed an increase in the value of R, and twelve of twenty observations showed an increase in the plasma chloride. In seven cases (1, 2, 9, 13, 24, 25 and 26), R and the plasma chloride increased together; in seven cases R increased while the plasma chloride decreased (5, 7, 8, 16, 17, 19 and 21), and five cases (4, 11, 18, 20 and 22) showed a decrease in R with an increase in plasma chloride. Irrespective of these changes, the administration of saline by increasing the fluid of the blood lowered the hemoglobin content in unit volume. In cases 1, 10, 11, 13, 15 and 25, the hemoglobin diminished from 10 to 20 per cent in two or three days. During this period, as a rule, the relative red cell volume diminished as well.

By the time the patient appeared to have recovered from his malady, the blood had become nearly normal. Thus, the alkali reserve was normal in nearly every case; the chloride was normal in fourteen of sixteen cases, and low in the remaining two; R had also become normal in all but four cases. The amount of hemoglobin and the hematocrit reading were usually decreased. In cases 7, 8, 13, 14, 15, 25 and 26 the decrease in the amount of hemoglobin was over 10 per cent. This fact supports the view that marked dehydration is present in the untreated case, but that when vomiting has ceased, the blood volume is quickly restored to normal. In cases 1, 10, 13 18, 21 and 26, after the administration of saline the hemoglobin was actually lower than in the cured infant. This observation indicates that an actual excess of fluid had been introduced in the body. Of course, in the interpretation of changes in hematocrit and hemoglobin readings, it is necessary to take account of the natural tendency for them to diminish during the early months of life. However, this decrease is not very sudden after the

7. Bakwin, Harry, and Rivkin, Helen: The Estimation of the Volume of Blood in Normal Infants and in Infants with Severe Malnutrition, Am. J. Dis. Child. 27:340 (April) 1924.

first month, and observations at intervals of two weeks are not likely to differ by more than 5 per cent in normal infants. Therefore, it may be said that the frequent estimation of the hemoglobin in cases of vomiting, with or without diarrhea, gives much information concerning the passage of water to and from the blood, and therefore of dehydration on the one hand, and of hydration and edema, on the other. These indications are more sensitive than those derived from clinical examination alone.

COMMENT

Whatever may be the cause of the unusual distribution of chloride in pyloric stenosis, it will be clear that the estimation of plasma chloride alone does not give an adequate picture of chloride depletion. For it has been shown that not only is the amount of cell chloride lowered out of all proportion to the amount of plasma chloride, but also that the hematocrit reading is often increased, so that the red cells contribute more largely to the bulk of the blood than is usually the case. In case 1, the plasma chloride is normal, while the whole blood contains only 60 millimols, compared with the normal figure of 80; in case 24, the plasma chloride is 54 millimols and the blood chloride only 37 millimols. Hence, in cases of this type, it is desirable to estimate both the plasma and the cell chloride, or else the chloride content of the whole blood alone. But even the figures for plasma chloride and cell chloride or for whole blood chloride do not convey fully the extent of the loss of chloride, for the amount of chloride in the circulation is further decreased in proportion to the diminution in the total blood volume, resulting from the loss of fluid by vomiting.

Apart from the practical consideration, however, there are certain observations which call for further discussion, and while the explanation of some of them is evident, the causation of others is obscure.

The increase of plasma bicarbonate and p_H and the decrease of plasma chloride are due to the loss of sodium chloride and hydrochloric acid in the vomit. This has already been discussed elsewhere.[9]

The increase of hemoglobin in unit volume of blood is due to the loss of water in the vomit.

The relatively high hematocrit reading probably depends on the reduction in the blood volume by vomiting and to some extent also on the loss of salt, which often exceeds the loss of water, so that the osmotic pressure of the plasma falls. As the base inside the red cells cannot diffuse outward because the membrane of the cell is impermeable to cations, the osmotic equilibrium is restored by an inflow of water from the plasma, raising the osmotic pressure of the plasma, lowering the osmotic pressure of the red cell and increasing the cell volume at the expense of the plasma. There are other factors, such as the reaction

of the plasma, concerned in the distribution of cell and plasma water, but these are of less importance.

There remains the explanation of the decrease in R. The factors concerned in the ratio of cell and plasma chloride have been fully considered by Van Slyke [8] and Henderson.[6] They discussed, however, not the chloride in whole cell or whole plasma, but the amount of chloride in cell water and plasma water. In their experiments, the chloride and water content of cell plasma are estimated, and the ratio, which in this connotation is represented by a small "r", is that of chloride ions in cell and plasma water. Therefore, before the deductions of Van Slyke and Henderson can be applied to the present data, it is necessary to consider what is the relation of "r" to "R":

$$R = \frac{Cl_{cell}}{Cl_{plasma}}$$

while

$$r = \frac{\frac{Cl_{cell}}{H_2O_{cell}}}{\frac{Cl_{plasma}}{H_2O_{plasma}}} = \frac{Cl_{cell}}{Cl_{plasma}} \times \frac{H_2O_{plasma}}{H_2O_{cell}} = R \times \frac{H_2O_{plasma}}{H_2O_{cell}}$$

Therefore, r differs from R by the ratio of plasma water to cell water. Hence, it does not follow that because R is abnormal, r, which is the measure of the true ionic equilibrium, is altered to the same degree, for if the water ratio had altered, r might still fall within normal limits. Thus, if R altered from 0.5 to 0.35, r might remain constant, provided that the ratio of plasma to cell water changed by 40 per cent, corresponding to a decrease in the hematocrit reading from, for instance, 40 to 34 per cent. Such a shift in the amount of water is most improbable, and would be as hard of explanation as a corresponding shift in the value of r itself. But in fact, as has already been noted, when R is low, the hematocrit reading, so far from being decreased, is actually increased in some cases (cases 1, 6, 8, 19 and 25); nor in any individual case does an increase in the hematocrit reading always accompany an increase in R. Further, from a consideration of the hematocrit reading and the hemoglobin content in succeeding records of any single case, it can be shown that the ratio of cell water to plasma water varies by less than 10 per cent, a deduction that has been supported by direct gravimetric estimation in cases 2, 9, 12, 15, 19, 20, 22, 24 and 25, in which the ratio of plasma water to cell water equaled 1.4 ± 5 per cent. It is therefore probable that comparatively small changes in the distribution of water attend the altered distribution of chloride, and that these changes are not such as would tend to increase the ratio of ionized chloride, r, or to bring it within normal limits.

8. Van Slyke, D. D.; Wu, H., and McLean, F. C.: J. Biol. Chem. **61**:765, 1923.

Moreover, the ratio of plasma water to cell water in pyloric stenosis is within the limits observed in normal subjects, and in view of the fact that the experimental error in the gravimetric estimation of small quantities may itself be as wide as ± 5 per cent, it may be presumed that errors involved in the assumption that R and r are proportional are small in degree when compared with the variations in R itself.

If this assumption is accepted, it may be shown from the Donnan equation,[8] that in the cases in which R (and presumably r) is low, the p_H difference between plasma and cells is increased; in other words, when the cell chloride is relatively low, the cell tends to become relatively more acid.

The influence of the p_H of the blood on R is more significant. Van Slyke and his co-workers [9] reported a series of cases in which r showed variations from the normal. But they showed that the changed value of r depended on the altered reaction of the blood and could have been predicted from the p_H in each case. They pointed out that the most important factors in determining r are the p_H of the blood, the total base of the plasma and the hemoglobin concentration of the red cell. The latter factor itself depends on the hemoglobin content and the p_H of the cell, the amount of ionized hemoglobin increasing with the p_H.

As in the cases of Van Slyke and in those of Peters and his collaborators,[10] the hemoglobin content of the cells and the total base of the plasma rarely varied by more than 10 per cent, the value of r was determined chiefly by the p_H. It has already been shown that in the present series of cases, the p_H of collected pathologic blood is usually within 0.1 of collected normal blood, and in any case is rarely greater than 7.6. This could not account for a chloride ratio of less than 0.42. In those cases in which the p_H of collected blood is known, the value of R at p_H 7.4 has been calculated, the data of L. J. Henderson [6] being used. It will be seen that the calculated values for R at normal p_H (column 12 of the table) are often far below the calculated values of R obtained in the normal subjects at this p_H (from 0.46 to 0.56).

Van Slyke has shown that r varies directly as the base of the plasma, and inversely as the hemoglobin concentration of the red cell.

We have no complete figures for plasma base, but in the absence of excess organic acid in the plasma (as indicated by the absence of diacetic acid and lactic acid from the urine) and in the presence of normal or only slightly increased plasma phosphate (as shown by direct estimation), the sum of the bicarbonate radical, HCO_3, and chloride may

9. Hastings, A. B.; Sendroy, J. J.; McIntosh, J. F., and Van Slyke, D. D.: J. Biol. Chem. **79**:193, 1928.

10. Peters, J. P.; Bulger, H. A.; Eisenman, A. J., and Lee, C.: J. Biol. Chem. **67**:175, 1926.

be taken as roughly proportional to the base present. Inspection of the table, however, shows that there is no indication that R, which is proportional to r, is related to the sum of $HCO_3 + Cl$, for it frequently happens that an increase of HCO_3 and chloride is accompanied by a fall in R (cases 4, 5, 10, 14 and 20), and a decrease in the total plasma acids by a rise in R (cases 7, 8, 16, 17, 19 and 21). In case 6, a big rise in R is unaccompanied by any change in $HCO_3 + Cl$, while in case 19 (fifteenth and twenty-third) the reverse is the case. In case 21, the $HCO_3 + Cl$ first falls while R rises, and later rises while R falls. Similar observations occur in cases 22 (tenth and twelfth; eighteenth and twenty-third) and in case 26 (seventeenth and twenty-fourth; twenty-fourth and first).

It is conceivable that simultaneous changes in the hemoglobin concentration might modify the effect of the plasma base. However, there are insufficient data for calculating the hemoglobin concentration of the red cells and in the absence of these, it would be unprofitable to enter into further analysis of the table.

There are certain other conditions in which similar variations may be found in the ratio of cell and plasma chloride: R is often low in cases of diarrhea with alkalosis, in which the sum of HCO_3 and chloride may be low or high. Similarly, after copious subcutaneous infusions, the hematocrit reading may suddenly diminish, and the volume of the blood increase, as shown by changes in the amount of hemoglobin, sometimes with the appearance of frank edema. The chemical observations vary; if saline is injected, the plasma chloride is high, the cell chloride is normal, plasma $HCO_3 + Cl$ are increased and R is diminished. If much alkali has been given, the plasma bicarbonate is high and the plasma and especially the cell chloride low, while $HCO_3 + Cl$ is usually, but not always, increased and R is diminished.

CONCLUSIONS

1. In pyloric stenosis in infants, the plasma p_H and the plasma bicarbonate are normal or increased; the plasma chloride and cell chloride are often diminished.

2. The volume of the blood is often decreased, and the relative cell volume increased.

3. The amount of cell chloride is usually lowered to a relatively greater extent than the plasma, so that the ratio of cell to plasma chloride is less than normal.

The Medical Staff of the Infants Hospital have given us permission to publish these investigations of their cases.

THE USE OF PROFESSOR LOEWENSTEIN'S OINTMENT FOR ACTIVE IMMUNIZATION AGAINST DIPHTHERIA *

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American medical literature is full of reports concerning the use of toxin-antitoxin mixtures for active immunization against diphtheria. During the last few years reports concerning the use of toxoid have also appeared in the American literature (Ramon and Illingworth,[1] Zingher,[2] Fitzgerald,[3] Weinfeld and Cooperstock,[4] Schwartz and Janney,[5] and Dick and Dick[6]). We shall now report briefly our results obtained in active immunization of forty-seven children with Professor Loewenstein's ointment.

In 1928, Professor Loewenstein[7] produced an ointment containing the diphtheria toxin modified by the addition of formaldehyde and dead diphtheria bacilli. The ointment thus differed from the toxoid not only in its consistency, but in the fact that it contained dead diphtheria bacilli. Professor Loewenstein believe that a true diphtheria immunization must

* Submitted for publication, July 8, 1930.

* The ointment prepared by Professor Loewenstein is essentially a combination of diphtheria toxoid with dead diphtheria bacilli. It is not generally available in the United States.

1. Ramon, G., and Illingworth, H. G.: Diphtheria Prophylaxis in France: Experiments with Anatoxin Vaccination, J. A. M. A. **91**:1028 (Oct. 6) 1928.

2. Zingher, A.: Immunity Results with Diphtheria Toxoid (Modified Toxin) and One-Tenth L + Mixtures of Toxin-Antitoxin in Public Schools of New York City, Proc. Soc. Exper. Biol. & Med. **22**:462, 1924-1925.

3. Fitzgerald, J. G.: Diphtheria Toxoid as an Immunizing Agent, Ann. Clin. Med. **5**:870, 1927.

4. Weinfeld, G. F., and Cooperstock, M.: Comparative Effects of Diphtheria Toxoid and Toxin-Antitoxin as Immunizing Agents, Am. J. Dis. Child. **38**:35 (July) 1929.

5. Schwartz, A. B., and Janney, F. R.: The Comparative Value of Toxoid and of Other Agents in the Immunization of the Preschool Child Against Diphtheria, Am. J. Dis. Child. **39**:504 (March) 1930.

6. Dick, G. F., and Dick, G. H.: Immunization Against Diphtheria, J. A. M. A. **92**:1901 (June 8) 1929.

7. Loewenstein, E.: Ueber perkutane Immunisierung, Wien klin. Wchnschr. **42**:193, 1929.

be antibacillary as well as antitoxic. He rubbed this ointment into the skin of a number of guinea-pigs and later gave them large lethal doses of diphtheria toxin. While the control animals all died, those protected by the ointment all remained alive. One of his co-workers, Löwy,[8] then used this ointment on 176 children, and in 1929 reported that 68 per cent of these children had become Schick-negative. Of 39 children whose blood was studied for the antitoxin content, 33 showed at least one-thirtieth unit of antitoxin per cubic centimeter of blood, and 22 showed at least one-fifteenth unit per cubic centimeter of blood. In the same year, Baar and Grabenhofer[9] reported that of 110 children who received three inunctions, 56.8 per cent became Schick-negative within less than six weeks, and 71.6 per cent within four months after the last inunction. Except for the appearance of a few papules which quickly disappeared in 4 children, they observed no general reactions and no rise in temperature. In a recent letter, Professor Loewenstein informed us that during the last two years the various hospitals of Vienna used this ointment on over 6,000 children and that not a single one of these children subsequently had had diphtheria.

Encouraged by these reports, we decided to try this ointment on forty-seven children of one of the infant welfare stations of the city of Chicago. We are briefly reporting the results obtained.

TECHNIC

The Schick test was performed on each child before the inunctions were given and six weeks after the last inunction. Material for the Schick test was obtained from the city laboratory. Each child received also a control Schick test with heated toxin.

Forty-seven children showing positive reactions in the preliminary Schick tests were then given three inunctions, ten days apart. Our technic of application was as follows: The skin of the posterior portion of the chest was thoroughly cleansed with alcohol and dried with ether. The contents of the tube were then rubbed into the skin for from two to three minutes. The ointment was then allowed to dry for another five minutes, and the mother was told not to bathe the child for twenty-four hours.

Six weeks later another Schick test was performed.

OBSERVATIONS

Six weeks after the last inunction was given, twenty-six, i.e., 55.3 per cent of the children who had received three inunctions gave negative reactions to the Schick test.

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8. Löwy: Diphtherieschutzimpfung mit der Löwensteinschen Toxoidsalbe, Wien. klin. Wchnschr. **42**:233, 1929.

9. Baar, H., and Grabenhofer, A.: Ueber perkutane Immunisierung gegen Diphtherie nach Löwenstein, Ztschr. f. Kinderh. **48**:248, 1929.

Of the children immunized, eleven were aged from 12 to 18 months; six, from 18 to 24 months; thirteen, from 2 to 3 years; ten, from 3 to 5 years, and five from 5 to 10 years.

We observed no general or local reactions, and the mothers did not report any rise of temperature or indisposition on the part of the children.

The evident advantage of this method of immunization lies in its simple technic, absolute painlessness and the fact that it does not sensitize the patient to future injections of antitoxin. Still another advantage lies in its antibacillary properties. As is well known, a negative reaction in the Schick test is not an absolute indication of immunity to diphtheria. Professor Loewenstein believed that to produce a true immunity one must give the patient not only an antitoxic agent (toxin-antitoxin or toxoid), but also an antibacillary compound. If this is true, Professor Loewenstein's ointment, containing the toxoid, as well as dead diphtheria bacilli, adds another important factor in the attempted immunization of the populace against diphtheria. Of course, it must be remembered that our results were obtained six weeks after the last inunction, and that Baar and Löwy obtained about 70 per cent negative reactions to the Schick test within four months after the last inunction. It would thus appear that the average results obtained by the use of toxin-antitoxin mixtures are about the same as those obtained by the use of Professor Loewenstein's ointment. However, the number of children who gave negative reactions to the Schick test after the use of the ointment is considerably less than the number who gave negative reactions after the use of the toxoid. If future work fails to show a large number of children giving negative reactions to the Schick test following treatment with Professor Loewenstein's ointment, this method, the safest and most agreeable yet devised, would appear to be inferior to that employing the toxoid.

SUMMARY

1. Twenty-six, or 55.3 per cent, of forty-seven children who were given three inunctions of Professor Loewenstein's ointment for active immunization against diphtheria gave negative reactions to the Schick test within six weeks.

2. No local or general reactions were noted.

DIETARY PROTEIN AND BLOOD-CLOTTING FUNCTION *

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Nutrition affects the coagulability of the blood to the extent of causing persons to bleed or the blood to clot more readily during illness. The constituents of the blood in the well person are maintained more or less constant by the regulated buffering mechanisms, the equilibrium relationships of which are difficult to disturb. But the components of the blood in the sick person are more readily altered as a result of the lability of the buffering mechanisms in the body.

Healthy persons maintained on an adequate dietary have a stable blood system, the composition of the clotting components remaining constant. But persons who have been on a prolonged unbalanced dietary have a labile blood system the clotting components of which may be more readily altered in one direction or another. The determination of the clotting and bleeding times offers no definite index of the actual hemorrhagic status of the person. But determinations of the blood-clotting constituents reveal the nature of the alteration in clotting function, and hence offer a basis of recognition of early manifestations of potential hemorrhagic disease.[1]

The dietary approach to the alleviation of an unfavorable hemorrhagic status of a person is particularly applicable to the prevention of actual hemorrhagic disease. Deficiencies in one clotting component or another may be corrected by dietary measures during the potential stages of disease. Hemorrhagic disease is not primarily nutritional in origin, and during its fulminating course it obviously cannot be cured by diet. It is only when during the potential period there is early recognition of the deviation in the clotting mechanism that the dietary treatment becomes preventive of the disease.

In previous communications [1] we attempted to relate the content of protein and fat in the diet to the formation of the constituents of

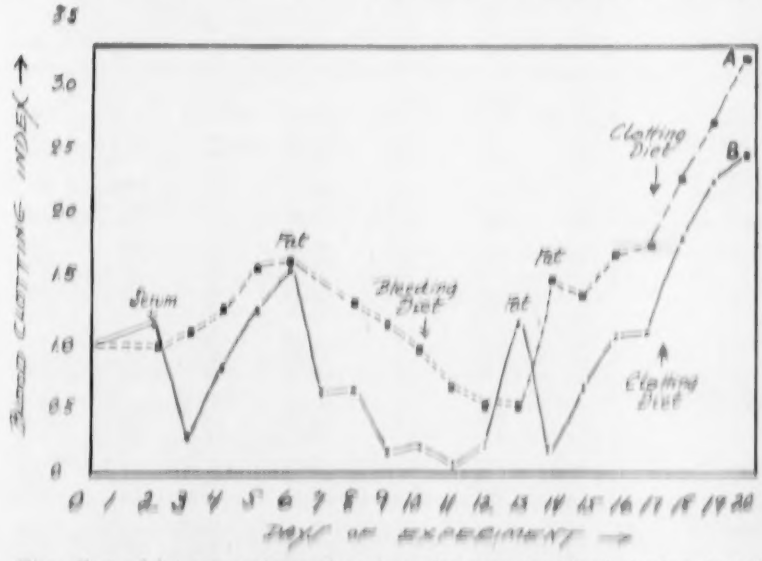
* Submitted for publication, July 28, 1930.

* From the Department of Pediatrics, the Fifth Avenue Hospital.

1. Bancroft, F. W.; Kugelmass, I. N., and Stanley-Brown, M.: Ann. Surg. **90**:161, 1929; The Determination and Regulation of the Blood Clotting Function in Childhood, Am. J. Dis. Child. **39**:471 (March) 1930. Kugelmass, I. N., and Tritsch, John E.: Prenatal Prevention of Potential Hemorrhagic Disease in the New-Born, J. A. M. A. **92**:531 (Feb. 16) 1929.

the blood that favor increased coagulability. On the other hand, we observed that the other dietary factors, carbohydrates and salts, were not productive of blood-clotting substances and hence favored bleeding. We wish to present some experimental data on the effect of a varied protein intake on the blood-clotting function.

Fibrin clot formation obtainable from the blood is increased with diets rich in protein; but those excessive in carbohydrates or fat result in a decrease of the formation of fibrin. Starvation leads to a low but constant fibrinogen level after the third day. Plethora induced by a transfusion of whole blood reduces the amount of fibrin obtainable, with a rapid return to normal.[2] The loss of fibrinogen by hemorrhage



The effect of intramuscular and oral nutrients on the blood-clotting function; *A* and *B* show the course of two dogs during a dietary experiment, with a rise in the blood-clotting index after an increase in the dietary protein.

results in its increase in twenty-four hours; in the dog the increase may lead to an excess of production followed by a return to normality. All evidence thus indicates that fibrinogen is rapidly utilized and produced from available globulins in the dietary. In fact, of all the plasma proteins, fibrinogen is the first to be replaced in the anabolism of body proteins.

Formation of fibrin may also be increased by the injection of heterologous proteins—serum, milk, gelatin, peptone—into the vascular system.[3] This mechanism is probably brought about by stimulation of

2. Foster, D. P., and Whipple, G. H.: Am. J. Physiol. **58**:365, 1922.
3. Lowry, J.: Zentralbl. f. inn. Med. **37**:833, 1916.

the production of fibrinogen rather than by the actual conversion of the introduced material into fibrinogen. Injury to the epithelium of the intestinal tract also causes overproduction of fibrin. A larger amount of fibrin is obtainable from the blood that is confined in veins isolated from the circulation than from the circulating blood. Fibrinogen is thus stored in the surrounding tissues and passes into the veins during stasis of the blood.[4] Surgical intervention, by direct stimulation of the clotting mechanism in the liver, is always conducive to an increase in the formation of fibrin.

For eight weeks animals were maintained on a basal dietary consisting of 15 per cent casein, 60 per cent dextrin, 15 per cent lard,

TABLE 1.—*The Effect of High Protein Diet on the Blood-Clotting Function*

Protein Source	Prothrombin	Fibrinogen	Antithrombin	Platelets	Lysis, per Cent	Index	Date
15% casein	0.4	0.10	8.5	565,000	45	0.014	8/26
	0.5	0.20	8.0	465,000	48	0.016	8/23
11% klim, 33% lima beans	0.5	0.2	8.0	535,000	53	0.016	8/27
33% klim	1.0	0.42	1.0	400,000	48	0.4	8/26
30% brain	1.0	0.36	1.0	120,000	30	0.35	9/ 6
	2.0	0.32	1.0	160,000	37	0.6	12/18
35% lung	1.0	0.32	1.0	100,000	30	0.3	9/ 6
	2.0	0.36	1.0	200,000	40	0.7	12/18
43% liver	1.0	0.28	1.0	570,000	54	0.3	8/29
	1.0	0.42	1.0	725,000	51	0.4	9/26
	1.0	0.40	1.0	670,000	45	0.5	11/27
33% klim, 66% whole wheat	1.0	0.42	1.0	560,000	50	0.4	9/26
	2.0	0.42	1.0	550,000	50	0.8	11/27
	2.0	0.42	1.0	650,000	52	0.8	1/20
35% beef	1.0	0.30	1.0	350,000	37	0.4	9/26
	1.5	0.42	0.75	360,000	30	0.8	11/27
	2.0	0.42	0.50	400,000	51	1.6	1/27
15% bone-marrow, 12% casein	1.0	0.42	1.0	650,000	46	0.4	9/26
	1.0	0.40	1.0	600,000	46	0.5	11/12
	2.0	0.54	0.5	500,000	50	2.1	1/27

4 per cent standard salt mixture, 3 per cent agar, 3 per cent yeast and 1 drop of viosterol and 5 drops of mineral oil. Quantitative determinations of the blood-clotting constituents were obtained in duplicate, and the regimen was changed to a diet with a high content of protein as indicated in the table of the results obtained. The animals were kept on this dietary for eleven weeks, and the blood determinations were repeated. The control group was maintained on a dietary consisting of 20 per cent casein, 54 per cent dextrin, 15 per cent butter fat, 2 per cent agar, 4 per cent salt and 5 per cent yeast. This experiment was initially carried out on an older group of animals and was subsequently repeated on twenty-four rats of weaning age, of an average weight

4. Plass, E. D., and Rourke, M. D.: J. Lab. & Clin. Med. **12**:735, 1927.

of 50 Gm., grouped in six cages and maintained on the foregoing dietaries.

A series of studies on the effect of diets high in protein content on the blood-clotting constituents were made on dogs by Dr. Stanley-Brown of the Department of Surgery. Initial blood determinations showed that the blood-clotting factors were identical qualitatively and

TABLE 2.—*Results of Blood Clotting Tests**

Dog	Diet	Prothrombin	Fibrinogen, per Cent	Antithrombin	Platelets	Index
1	Normal diet	1.11	0.64	1.16	200,000	0.6
	Carbohydrate and vegetable diet	1.11	0.64	1.16	200,000	0.6
	Protein diet	1.45	1.12	0.95	250,000	1.7
2	Normal diet	1.00	0.54	1.00	400,000	0.5
	Carbohydrate and vegetable diet	0.74	0.54	1.00	220,000	0.3
	Protein diet	1.00	0.64	1.00	300,000	0.7
3	Normal diet	1.11	0.64	1.16	220,000	0.6
	Carbohydrate and vegetable diet	1.11	0.28	1.00	135,000	0.3
	Protein diet	1.26	0.69	1.00	210,000	0.9
4	Normal diet	1.00	0.40	1.16	200,000	0.3
	Carbohydrate and vegetable diet	1.00	0.40	1.16	225,000	0.3
	Protein diet	1.11	0.64	0.95	330,000	0.7

* Composition of blood after a normal diet, after forty-eight hours on a carbohydrate and vegetable diet and after forty-eight hours on a visceral protein diet.

TABLE 3.—*The Effect of a Surgical Operation on the Blood-Clotting Function*

Patient	Prothrombin	Fibrinogen	Antithrombin	Platelets	Lysis, per Cent	Index	Date	Operation	Diagnosis
K. B.	1.0	0.74	1.0	160,000	26	0.7	4/26	Pre	Fibroids
	1.0	1.30	1.0	170,000	29	1.3	5/12	Post	Endocarditis
M. D.	1.0	0.59	1.0	200,000	22	0.6	5/ 3	Pre	Anal prolapse
	1.4	1.08	1.0	165,000	27	1.4	5/ 8	Post	
F. H.	1.0	0.64	1.0	230,000	34	0.6	4/ 5	Pre	Adenoma of thyroid
	1.0	2.62	1.0	205,000	39	2.6	4/12	Post	
C. S.	1.0	0.64	1.0	305,000	42	0.6	4/ 2	Pre	Cholecystitis
	1.0	1.62	1.0	275,000	30	1.6	4/ 7	Post	
C. G.	1.0	0.64	1.0	325,000	43	0.6	4/ 3	Pre	Appendicitis
	1.0	1.84	1.0	240,000	35	1.8	4/ 7	Post	

quantitatively with those obtained from children. The animals were at first maintained on the usual dietary; then they were placed on a regimen consisting essentially of carbohydrates and vegetables, and blood was taken. Finally, they were placed on a diet high in protein content, and the blood determinations were made in forty-eight hours. In the course of this experimental work on the dietary treatment for potential hemorrhagic disturbances, we consistently observed a definite alteration in the clotting factors following a surgical operation. Some typical data are taken from the results obtained in Dr. Bancroft's surgical service.

CONCLUSIONS

1. Prolonged feeding of a diet containing protein increases the coagulability of the blood, maintaining the clotting factors at a higher level.

2. Injury of the tissues by surgical intervention induces an overproduction of blood fibrinogen and hence an increased coagulability of the blood.

3. The introduction of heterologous protein into the vascular system increases the blood-clotting function transiently, with a rapid return to normal.

INTRAPERITONEAL IRON *

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AND
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The use of iron as a therapeutic agent in the treatment for anemia and debilitating conditions is one of the oldest of therapeutic measures. Beginning with the end of the last century, workers began to study its physiologic action. In 1880, Gottlieb [1] administered iron subcutaneously to study its action; he found that 70 per cent was excreted in the feces. Ziegler,[2] using the same method, found iron only in the Kupffer cells of the liver, and Hoffman [3] showed that the administration of medicinal preparations of iron lead to its accumulation in the liver and spleen. In 1900, Cloetta [4] first demonstrated that the absorption of iron takes place from the duodenum.

In 1928, Polson [5] contributed his classic studies on the fate of colloidal iron administered intravenously. After injection into rabbits, he found iron in the Kupffer cells of the liver from one minute to nine days before it was present in the liver cells. In brief, his observations were that in rabbits the iron was found in the lungs, liver and spleen; in the lungs it occurred as emboli in the vessels; in the liver and spleen it was ingested by the endothelial cells. When the Kupffer cells are charged with iron they tend to be detached from the capillary walls and congregate in the lumina; later they fuse and form multinucleated giant cells. Iron was not found in the epithelium of the kidney tubules until the second week. It was not found in the bone-marrow. It was excreted by the cecum.

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* Read before the Section on Diseases of Children, at the Eighty-First Annual Session of the American Medical Association, Detroit, June 27, 1930.

* From the Department of Pediatrics, Rush Medical College of the University of Chicago, and the Presbyterian Hospital of Chicago.

1. Gottlieb, R.: Ueber die Ausscheidungsverhältnisse des Eisens, Ztschr. f. physiol. Chem. **15**:371, 1891.

2. Ziegler, E.: Zur Kenntnis der Eisenablagerungen, Centralbl. f. allg. Path. u. path. Anat. **5**:847 (Oct.) 1894.

3. Hoffman, A.: Die Rolle des Eisens bei der Blutbildung, Virchows Arch. f. path. Anat. **160**:235 (May 14) 1900.

4. Cloetta, M.: Kann das medicamentöse Eisen nur in Duodenum resorbiert werden? Arch. f. exper. Path. u. Pharmakol. **44**:363 (Aug. 23) 1900.

5. Polson, J.: The Fate of Colloidal Iron Administered Intravenously, J. Path. & Bact. **31**:445 (July) 1928; **32**:247 (Feb.) 1929.

It occurred to us that the intraperitoneal injection of colloidal iron might offer a safe and easy means of introducing iron into the organisms. The following experiments were carried out on animals:

METHOD

Metallic iron in the colloidal state, as ferric hydroxide, was injected intraperitoneally into rabbits. The solution contained 1.5 mg. of colloidal iron to each cubic centimeter, and the amounts given ranged from 1.5 to 25 mg. per kilogram of body weight.

The histologic sections were fixed in a diluted solution of formaldehyde, U. S. P. solution (1:10), and passed through fresh 2 per cent solutions of potassium ferrocyanide and hydrochloric acid. The sections were counterstained with neutral red.

The chemical examinations were made by mincing the organs on glass slides, washing them several times with water and drying to a constant weight at 100 C. They were then analyzed by Kennedy's [6] process, and the iron estimated according to the procedure used by Elvehjem and Hart.[7]

Results of the Experiment

	Normal—5 Rabbits: Total Mg. of Iron	Iron Injection—14 Rabbits		
		Dosage, Mg.	Time, Weeks	Total Iron
Liver	2.85 to 9.55	15	1	4.66 to 9.0
		60	4	10.56 to 14.95
		120	8	28.85 to 88.45
		180	12	55.85 to 60.05
Spleen	0.85 to 2.05	15	1	0.85 to 2.2
		60	4	1.0 to 1.09
		120	8	0.06 to 1.54
		180	12	1.0 to 2.0

In the histologic study it was found that the iron proceeds from the peritoneal cavity by two routes. A considerable part is taken up by the lymph glands of the mesentery and passes into the thoracic duct. Another part is taken up by the macrophages as a glutinous material in the peritoneal fluid, and is deposited on the mesentery and peritoneal organs. This part eventually penetrates between the endothelial cells and enters the lymphatic vessels of the subserous tissue. A large amount of this iron is eliminated through the cecum. Iron is found in the Kupffer cells in about seven days, but it does not appear in the liver cells until forty-five days. The iron appears in the cells at the periphery first, and spreads toward the center later. During this process, the Kupffer cells appear to loose their charges of iron. The amount of the total dosage does not affect the time of appearance of the iron in the liver. No iron was deposited in the spleen.

6. Kennedy, R. P.: Quantitative Determination of Iron in Tissue, J. Biol. Chem. **74**:385 (Aug.) 1927.

7. Elvehjem, C. A., and Hart, E. B.: Iron Determination in Animal Tissue, J. Biol. Chem. **67**:43 (Jan.) 1926.

Daily estimations of hemoglobin and red cells were made on the blood of the animals. There was no particular change in the hemoglobin or red cells in animals given colloidal iron. Those made anemic by bleeding did not regenerate any faster after intraperitoneal injections of iron than those that did not receive it.

CLINICAL CASES

As there were no harmful reactions, treatment was begun on a series of children. The method adopted was to inject 5 cc. of colloidal iron as ferric hydroxide, the solution containing 8 mg. of colloidal iron.

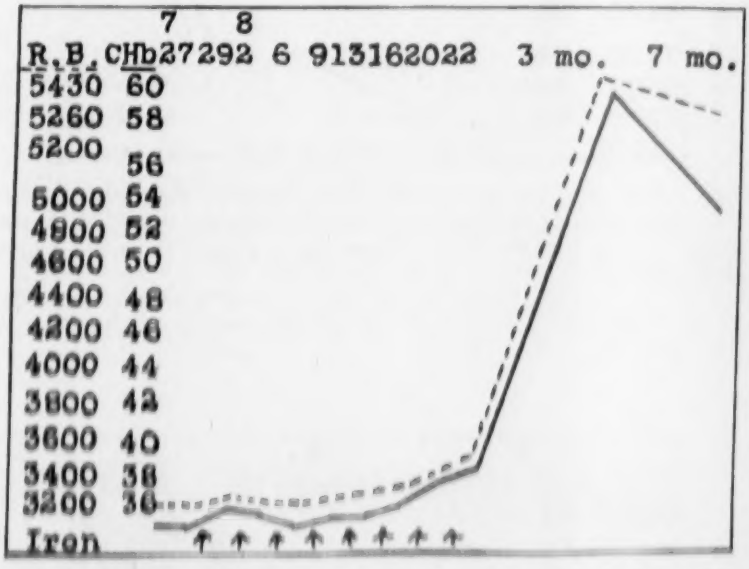

Chart 1 (case 1).—The patient's age was 10 months. Secondary anemia following malnutrition and pertussis. Weight on entrance, 11 pounds, 13 ounces (5,414.77 Gm.). Weight on discharge, 12 pounds, 11 ounces (5,759.94 Gm.).

This standard amount was used irrespective of the weight of the child. These injections were given twice a week for eight injections. The method of injection was that described by Sanford.[8]

The cell counts were made in the usual manner, and the hemoglobin was estimated by the Newcomer method, the standard being checked as described by Sanford.[9]

8. Sanford, H. N.: Treatment with Intraperitoneal Injection of Neoarsphenamin, J. A. M. A. 85:242 (July 25) 1925.

9. Sanford, H. N.: Effect of Ultraviolet Light on the Blood of New-Born Infants: II. Erythrocytes and Hemoglobin, Am. J. Dis. Child. 35:9 (Jan.) 1928.

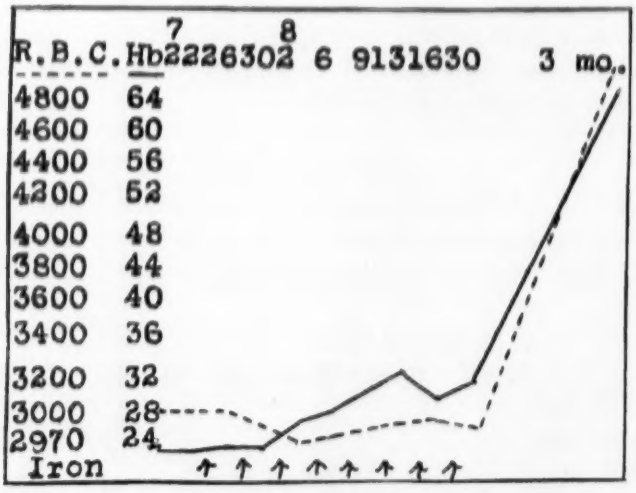

Chart 2 (case 2).—The patient's age was 13 months. Congenital inferiority, and secondary anemia following rickets and malnutrition. Weight on entrance, 12 pounds 14 ounces (5,840 Gm.) Weight on discharge, 13 pounds 2 ounces (5,953.40 Gm.).

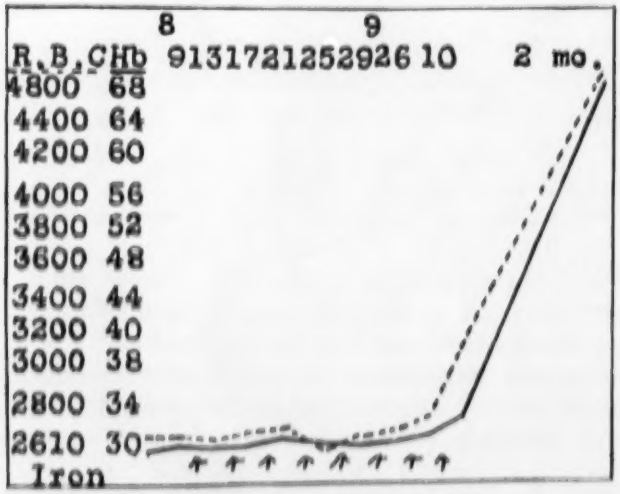

Chart 3 (case 3).—The patient's age was 2 years. Secondary anemia following rickets and malnutrition. Weight on entrance, 19 pounds, 7 ounces (8,816.69 Gm.). Weight on discharge, 21 pounds (9,525.42 Gm.).

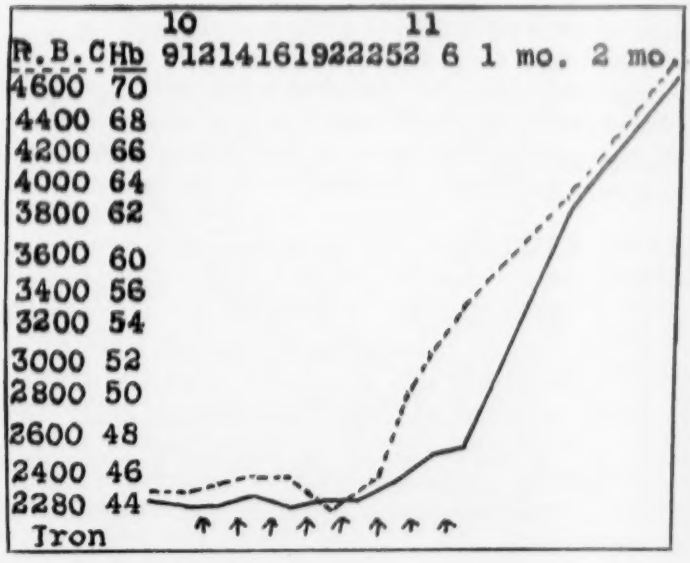

Chart 4 (case 4).—The patient's age was 15 months. Secondary anemia following rickets and bronchitis. Weight on entrance, 16 pounds 8 ounces (8,397.45 Gm.). Weight on discharge, 17 pounds 12 ounces (8,051.26 Gm.).

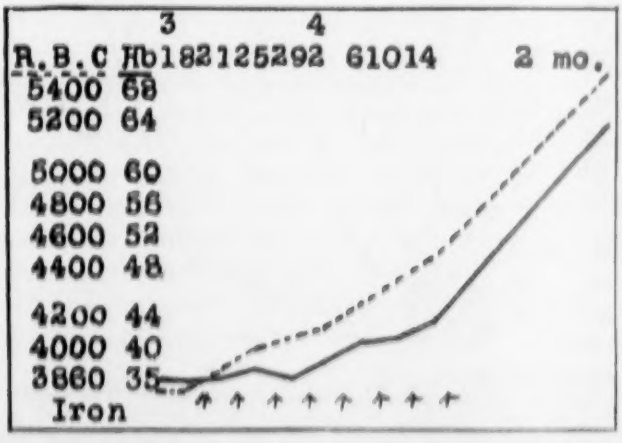

Chart 5 (case 5).—The patient's age was 10 months. Secondary anemia following intermittent vomiting, anorexia and asthmatic bronchitis. Weight on entrance, 15 pounds, 7 ounces (7,002.33 Gm.). Weight on discharge, 16 pounds (7,257.48 Gm.).

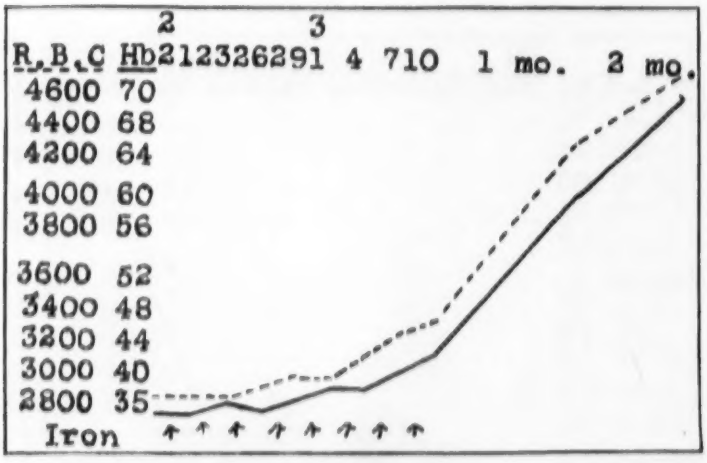

Chart 6 (case 6).—The patient's age was 9 months. Secondary anemia following prematurity and malnutrition. Weight on entrance, 10 pounds, 2 ounces (4,592.62 Gm.). Weight on discharge, 11 pounds, 8 ounces (5,216.32 Gm.).

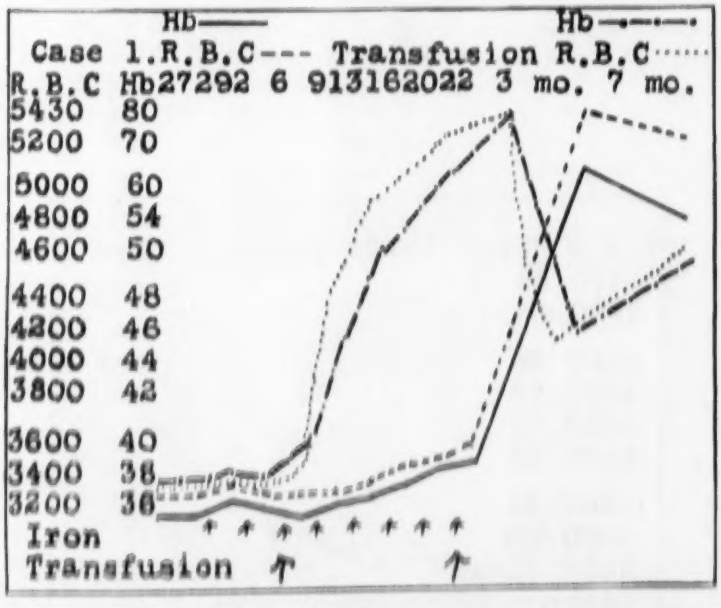

Chart 7.—Comparison of case 1 with that of patient's twin brother, who received two intraperitoneal transfusions of whole blood. Control case. Secondary anemia following malnutrition and pertussis. Weight on entrance, 12 pounds, 2 ounces (5,499.80 Gm.). Weight on discharge, 13 pounds, 4 ounces (6,010.10 Gm.).

COMMENT

It will be observed from the accompanying charts that there is little or no rise in the hemoglobin or red cells during the time of injection, or about thirty days. Following this time there is a rise of hemoglobin to the amount of 5 per cent (Newcomer) a week. It is the general idea that secondary anemia is due more to an inability to use the iron taken in or stored in the body than to a mere lack of iron. The administering of therapeutic iron therefore simply creates a reservoir on which the body may draw.

In our series of cases all of the patients received ultraviolet irradiation to assist the body in its assimilation of iron. Our method was to expose the front and back of the body, beginning with a three minute exposure and increasing the time one minute a day until an exposure of ten minutes was given. Irradiation was then stopped. In later cases, which will be reported, one or two injections of whole or citrated blood are given intraperitoneally to cause the same effect. In chart 7 a control case is shown in comparison with case 1. These twins were about the same weight, and the observations on their blood were similar. The control subject was rapidly benefited after two intraperitoneal transfusions of whole blood, but after three months his physical condition had fallen below that of the child given iron intraperitoneally. After seven months his condition was still below that of the other child.

The child remains under observation in the hospital during the month of treatment. After this he is sent home, and the blood is checked at monthly intervals. The patients in the first two cases are still in good condition after eight months, so the results appear permanent.

No effect or reaction was noted with the dose given. In the child aged 2 years in the preceding series, two doses of 10 cc. each were given, and each time a rise in temperature of 2 degrees was noted within six hours after injection. This did not occur after the reduction of the dosage to 5 cc. It was thought that larger doses might cause more stimulation, as Waddell, Steenbock and Hart [10] found that small doses of iron were ineffective in causing any change, whereas larger doses stimulated the formation of hemoglobin. They expressed the belief that this was due to minute traces of copper.

In the first few treatments iron cacodylate was used, but its use was discontinued. No difference was observed. Goerner [11] found that in

10. Waddell, J.; Steenbock, H., and Hart, E. B.: The Ineffectiveness of High Doses of Iron in Curing Anemia in the Rat, J. Biol. Chem. 88:242 (July) 1929.

11. Goerner, A.: The Effect of Colloidal and Crystalloidal Metallic Compounds in Nutritional Anemia in the Rat, J. Lab. & Clin. Med. 15:119 (Nov.) 1929.

the rat crystallous compounds rapidly cured nutritional anemia, whereas colloid compounds had no effect.

This form of treatment is successful only in secondary anemia. It was tried in a case of primary anemia, with no effect on the hemoglobin or red cells. The same patient did not respond to transfusion of blood or to the administration of liver extract.

CONCLUSIONS

Intraperitoneal injection of iron in doses of 5 mg. at three day intervals, combined with ultraviolet light or with one or two transfusions of blood, seems to be of value in the treatment of children with secondary anemia.

It apparently has no effect on the hemoglobin or red cells in primary anemia.

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ABSTRACT OF DISCUSSION

DR. W. C. C. COLE, Detroit: This work is interesting, especially in relation to the study of the fate of iron in the body and the absorption of foreign material from the peritoneum. Whether or not this rather unusual method of giving iron in the treatment for anemia has any particular merits over the simpler methods more commonly used will require further study. Every one uses iron in the treatment for anemia, and one frequently is disappointed in the results obtained. This accounts for the wide variety of forms of iron and the methods of administration, and for the continued search for newer and better ways of giving this element. It seems obvious that the failure to get good results with iron therapy is not due to the form of iron used, or to the method of administration, but to the fact that nutritionally iron plays little or no part in many anemias of childhood. Anemia has come to be regarded as a symptom nearly as general in its etiology as fever or vomiting. To search for a universal therapeutic agent is as futile in anemia as in those other conditions. A large proportion of the anemias in children, at least in this part of the country, are not due to deficiency in diet or in iron, but to metabolic and constitutional disease and infection, especially septic infection. Iron therapy in this type of anemia is largely futile unless the etiologic agent is first removed. In our experience with these septic anemias, the only therapeutic agent of any particular value, while the process is still active, is blood transfusion. This is so easily applied and requires such a short time to get a prompt therapeutic effect that one should not hesitate to use it frequently. One fact that should be emphasized is the time element required in the treatment for anemia. Even in the most favorable type of deficiency anemia, four or five weeks' treatment is required to produce a satisfactory effect. During the winter and spring months in the northern climates, the danger of secondary infection from respiratory or contagious disease is so great that if one can cure these cases of anemia in a short time, it seems foolish to take the risk that goes with prolonged medical treatment.

This work of Dr. Grulee and Dr. Sanford possibly is open to the criticism that they have introduced quite a few variables in their work. In addition to the treatment with iron they have used blood transfusion and treatment with light. No mention was made as to the dietary regimen that the children were given. These factors are all important. I have very little faith in treatment with iron for the anemia of children. If good diet and hygiene do not take care of the situation, there is usually something else the matter with the child.

Dr. H. N. Sanford, Chicago: Everything Dr. Cole said is true. We never used iron in the treatment for anemia in children until our laboratory experiments showed that it was justified. As to the anemia being due to a deficiency in iron, that is correct. What we are trying to do is to create a reservoir from which the body can draw the iron as it needs it. Of course, if the organism is unable to draw this iron, the reservoir will be of no use. Blood transfusions are, of course, very rapid and effective. Our point is that its benefits will last only a short time. For example, in the control case we have shown, the benefits apparently lasted only one month. Our idea is that one or two blood transfusions should be given during the first month, and that the child should be given injections of colloidal iron as well. The immediate results are from the blood transfusion and the later ones are from the colloidal iron. Diet and light are important factors. If a child is suffering from secondary anemia caused by undernutrition, and he is given a proper diet, obviously there will be some temporary increase in the hemoglobin and red cells. When the child goes back to his former surroundings the condition of the blood will reappear. This happened in the case that was studied for seven months. There had been a slight drop at the end of three months, but not so much as in the case in which the patient received the intraperitoneal blood. No reactions were observed, with the exception of the one case in which there was an elevation of temperature of 2 degrees when we doubled the dose of iron. This child was twice as heavy as the other infants and was given twice as much iron. If one continues the dosage of 5 cc. or 8 mg. of colloidal iron, there is absolutely no danger.

RICKETS

THE COMPARATIVELY HIGH VALUE OF COLORADO SUNSHINE IN ITS PREVENTION *

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AND
ROBERT C. LEWIS, PH.D.
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A thorough survey of the literature shows certain outstanding milestones in the progress toward the present knowledge of rickets. This has been so widely disseminated that it is necessary only to recall the names and contributions of the men concerned with it. Between the first work done by Glisson [1] on etiology in 1650 and that of Mellanby [2] in 1918 on an antirachitic factor or vitamin, there is a long lapse of time with little in the way of contributions to knowledge concerning the etiology of rickets. Following this, progress has been rapid and constructive. The demonstration by Huldschinsky [3] in 1919 of the curative action of ultraviolet rays of the mercury vapor quartz lamp was followed by the observation of Hess and Unger [4] in 1921 that sunshine had a similar action in infantile rickets. The following year, McCollum, Simmonds, Becker and Shipley [5] submitted proof of the existence of vitamin D, and that cod liver oil was its most concentrated source. In 1925 three separate groups of investigators, Rosenheim and Webster [6] in England, and Hess, Weinstock and Helman [7] and Steenbock and Black [8] in the United States, found that inert food containing cholesterol or allied substances could be activated by ultraviolet rays and thus be given the antirachitic property. More recently, it has been shown

* Submitted for publication, July 11, 1930.

* From the Departments of Biochemistry and Pediatrics, University of Colorado School of Medicine.

* Reported before the Division of Biological Chemistry at the meeting of the American Chemical Society, Columbus, Ohio, May 1, 1929.

1. Glisson, F.: De rachitide, London, G. Du-Gardi, 1650.

2. Mellanby, E.: J. Physiol. **52**:11, 1918; Lancet **1**:407, 1919.

3. Huldschinsky, K.: Deutsche med. Wchnschr. **45**: 712, 1919.

4. Hess, A. F., and Unger, L. J.: Cure of Infantile Rickets by Sunlight, J. A. M. A. **77**:39 (July 2) 1921.

5. McCollum, E. V.; Simmonds, N.; Becker, J. E., and Shipley, P. G.: J. Biol. Chem. **53**:293, 1922.

6. Rosenheim, O., and Webster, T. A.: Lancet **1**:1025 (May 16) 1925.

7. Hess, A. F.; Weinstock, M., and Helman, F. D.: J. Biol. Chem. **68**:305, 1925.

8. Steenbock, H., and Black, A.: J. Biol. Chem. **64**:263, 1925.

by Hess and Windaus[9] and by Rosenheim and Webster[10] that it is not cholesterol but ergosterol, a contaminant of cholesterol, that is the substance activated. Five mg. of activated ergosterol produces the same antirachitic effect as 1 liter of active cod liver oil.

The preventive and curative value of light in rickets has been investigated rather extensively both in this country and abroad. In 1890 Palm[11] suggested the importance of sunlight in the prevention and cure of rickets, but it was Huldschinsky[8] who first proved the relationship of ultraviolet light to rickets. He wrote: "The therapeutic effect of quartz light irradiation is invariably apparent in all forms of rickets. Recovery results more promptly than with any of the methods employed heretofore. The effects of irradiation are lasting, and the regenerative process is active for at least two months after interruption of the treatment." The ultraviolet waves that have been found to be effective have been obtained from the solar spectrum, from the mercury vapor lamp and from the carbon arc lamp.

Hess and Weinstock[12] called attention to the fact that in using ultraviolet light rays in the prevention and cure of rickets in experimental rats the wave length has a determining effect on the beneficial quality of the result. To be beneficial the waves must have a length not greater than 302, or possibly 313, millimicrons. The shortest ultraviolet rays of the sun to reach the earth under the most favorable conditions are about 290 millimicrons, varying in intensity according to the time of day, to the season of the year and to the condition of the atmosphere. If the air is heavy with moisture or polluted with smoke and dust, waves shorter than 300 or even 313 millicrons may be absorbed. Hess, Unger and Pappenheimer[13] used Pappenheimer diet no. 84, and exposed rats to sunlight in April for a period of from fifteen to thirty minutes four or five days a week; they found that rickets did not develop after from thirty-two to thirty-five days, whereas the animals kept in absolute darkness showed marked rickets.

Powers, Park, Shipley, McCollum and Simmonds[14] fed rats on McCollum diet no. 3143 and exposed them for a total of 242 hours

9. Hess, A. F., and Windaus, A.: Proc. Soc. Exper. Biol. & Med. **24**:461, 1927.

10. Rosenheim, O., and Webster, T. A.: Biochem. J. **21**:389, 1927.

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12. Hess, A. F., and Weinstock, M.: Study of Light Rays in Their Relation to Rickets, J. A. M. A. **80**:687 (March 10) 1923.

13. Hess, A. F.; Unger, L. J., and Pappenheimer, A. M.: J. Biol. Chem. **80**: 77, 1922.

14. Powers, G. F.; Park, E. A.; Shipley, P. G.; McCollum, E. V., and Simmonds, N.: Prevention of Development of Rickets in Rats by Sunlight, J. A. M. A. **78**:159 (Jan. 21) 1922.

over a period of 62 days; they found that no rickets had developed, whereas in control animals fed the same diet but kept under conditions of ordinary room light rickets did develop.

Hess [15] found that in rats exposed to sunlight behind a quartz pane in September for an hour daily rickets did not develop even though a rickets-producing diet was given. In a later paper [16] he reported that direct sunlight for fifteen minutes daily was protective, but reflected sunlight for the same length of time afforded incomplete protection. Webster and Hill,[17] working in England, concluded that a minimum exposure of two hours to bright sunshine or skyshine five days a week was necessary to protect rats from rickets under the same severe experimental conditions. Sabatini [18] found that in rats kept on Pappenheimer diet no. 84 and exposed to sunlight for ten minutes daily rickets developed. Tisdall and Brown,[19] utilizing December sunlight in Toronto, found that it had a definite antirachitic effect on rats fed a rachitogenic diet (McCollum diet no. 3143). Roentgenograms of rats exposed to direct sunlight for two hours showed only from a slight to a moderate degree of rickets, whereas those of rats exposed from one-quarter to one hour showed marked rickets.

The object of the experiments herein reported was to ascertain the minimum amount of sunlight required to prevent the development of rickets in rats. As a review of the literature failed to reveal that any work had been done to determine this point, the subject seemed well worth investigating.

EXPERIMENTAL PROCEDURE

Fourteen male albino rats, between 20 and 22 days of age, and weighing from 30 to 36.5 Gm., were placed on distilled water and McCollum diet no. 3143 consisting of: whole wheat kernel, 33 per cent; whole maize kernel, 33 per cent; gelatin, 15 per cent; wheat gluten, 15 per cent; sodium chloride, 1 per cent, and calcium carbonate, 3 per cent.

In our preliminary work we had employed a number of the diets that have been perfected to produce experimental rickets in rats with changes in the bones and blood identical with those seen in rachitic infants, but as we had found the McCollum diet most satisfactory, we adopted it for use in our experimental work.

The rats were divided into seven groups of two rats each. The largest and smallest with a difference in weight of 6.5 Gm. were taken as controls, and were kept in the dark continuously in order to make sure that they would not

15. Hess, A. F.: Ultraviolet Rays of Sun, J. A. M. A. **84**:1033 (April 4) 1925.

16. Hess, A. F.: Newer Aspects of Rickets Problem, J. A. M. A. **78**:1177 (April 22) 1922.

17. Webster, A., and Hill, L.: Brit. M. J. **1**:956, 1925.

18. Sabatini, S.: Policlinico **33**:147, 1926.

19. Tisdall, F. F., and Brown, A.: Proc. Soc. Exper. Biol. & Med. **24**:446, 1927.

receive any ultraviolet irradiation. The other animals were grouped in pairs, according to weights, and the variations in any individual group did not exceed 0.5 Gm., except in one case in which there was a difference of 1 Gm.

The animals were kept in a dark room in individual wire-meshed screen cages, like those employed by Osborne and Mendel (compare Ferry[20]). The dark room was immediately adjacent to the hospital roof on which the animals were exposed. No daylight was permitted to enter, this being prevented by a double door and a double covering of beaverboard over the windows, so placed that free ventilation was permitted. When necessary, interior illumination was provided by a red light. Wooden carriers constructed to hold three inverted cage tops each (fig. 1) were used to transport the rats from the dark room to the roof. The carriers were covered with dark cloths during the transfer in order

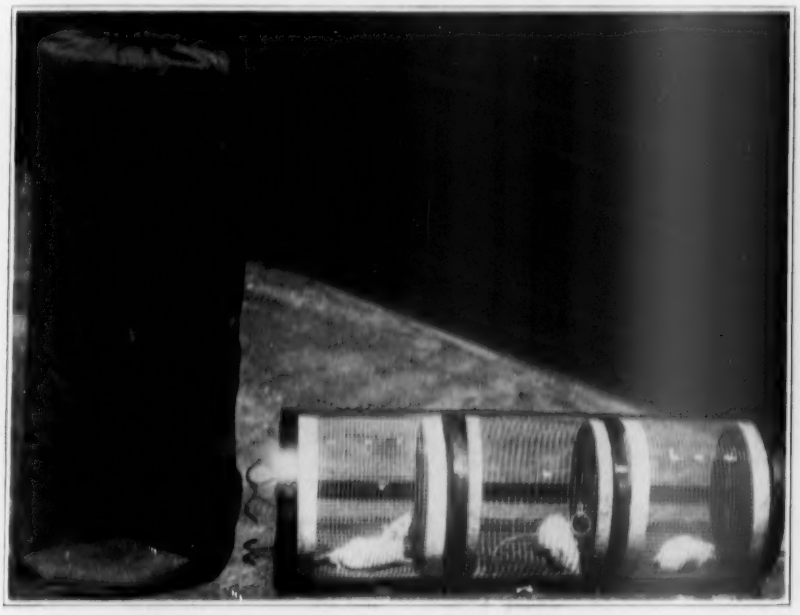

Fig. 1.—Two views of cage carrier used for transporting rats to roof for exposure to sunlight. At left, carrier with dark cloth cover; at right, rats being exposed to sunlight.

that no sunlight could reach the animals except during the period of exposure to sunlight.

The period of experiment was forty days, beginning on June 3, and ending July 13, 1927. The controls were kept in the dark throughout the experiment; the others were exposed to the direct sunlight for periods varying from 2.5 to 15 minutes by intervals of 2.5 minutes each day that the sun shone except three. No definite time of day was used for the exposure to sunlight, but in all except four instances insolation occurred between 9:30 a. m. and 1:45 p. m. Twice the exposure was made at 8:45 a. m., once at 9:00 a. m. and once at 4:30 p. m.

20. Ferry, E. L.: J. Lab. & Clin. Med. 5:735, 1919.

The animals were exposed for thirty of forty days (75 per cent) except in the case of rat 103 which was found dead on the morning of the twenty-fourth day and, consequently, was exposed only eighteen of twenty-three days (78.26 per cent).

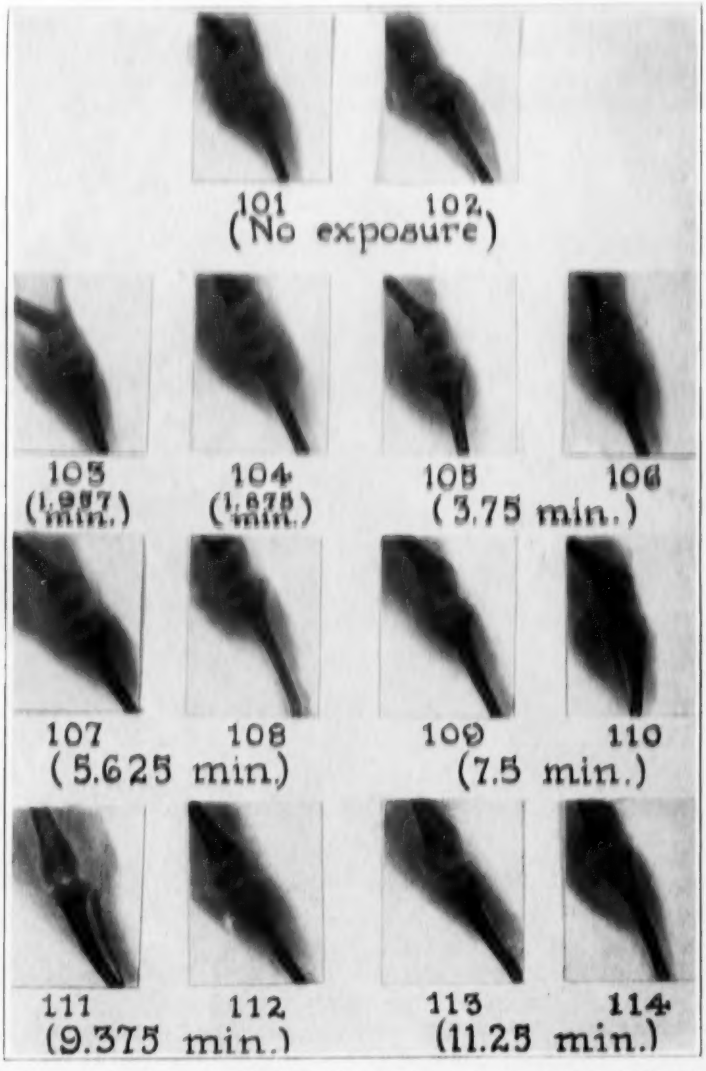

Fig. 2.—Roentgenograms of tibiae of experimental rats (101 to 114), showing antirachitic effect of short exposures to sunshine. (Figures in parentheses give average daily exposure to direct sunshine.)

The animals were weighed every third day. At the end of the period the animals were killed by ether anesthesia and eviscerated. Roentgenograms of the entire body were made, great care being taken to place the animals on the film

so that a similarity would exist when like parts were studied. The bodies were then immersed in a diluted solution of formaldehyde (1:10) and used later for a study of the ash content of the bones. The interpretation of the presence or absence of rickets was obtained by studying the degree of calcification in the proximal ends of the tibia and humerus, in which the metaphyses are wider than in others bones, and from the percentage of ash content of these same bones.

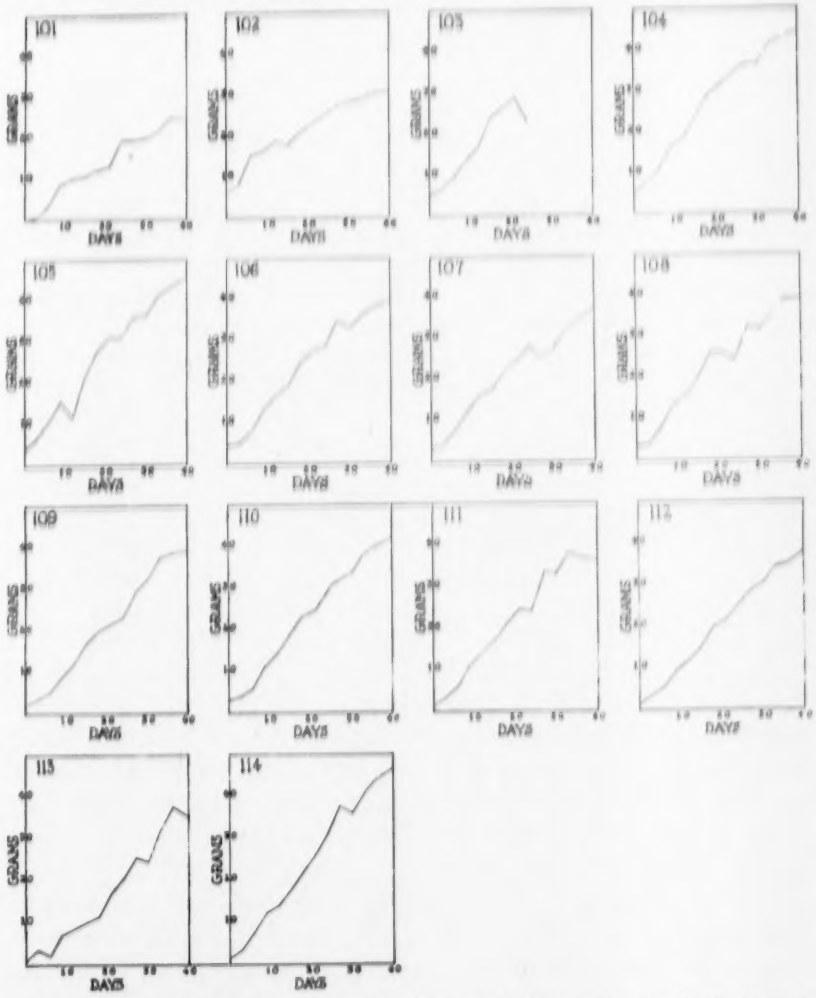

Fig. 3.—Growth curves of rats showing retarded growth of animals kept in dark (rats 101 and 102) as compared with growth of animals receiving short exposures to sunlight (from 1.875 minutes daily for rat 104 to 11.25 minutes daily for rats 113 and 114).

Although roentgenograms were made of the entire rat, and both the humerus and the tibia were studied, reproductions of the latter only are included here, as the observations in both cases give concordant results.

RESULTS OF THE EXPERIMENT

Figure 2 shows definitely our experimental observations in regard to the antirachitic action of sunlight as judged by the roentgenographic method. It will be observed that in the control rats, 101 and 102, which were kept in the dark, rickets developed to a marked degree. Rat 103, exposed to direct sunlight for an average of 1.957 minutes daily showed well developed rickets after 23 days. Rat 104 was not killed until the end of 40 days after being exposed for an average of 1.875 minutes daily. This rat showed as marked a rachitic condition as the controls. A somewhat lesser degree of rickets is seen in rats 105 and 106 in which the average daily exposure was 3.75 minutes. The next group (rats 107 and 108) with an exposure of 5.625 minutes daily received even greater protection, although definite rickets

The Antirachitic Effect on Rats of Exposure to Sunshine for Varying Lengths of Time Daily, from June 3 to July 13, Inclusive

Rat	Average Daily Exposure to Sunshine for 40 Days, Minutes	Ash Content of Femur and Tibia, per Cent	Degree of Rickets as Judged by Roentgenograms
101	0	18.66	Marked
102	0	24.63	Marked
103*	1.957	39.88	Moderate
104	1.875	24.66	Marked
105	3.75	34.15	Moderate
106	3.75	37.50	Moderate
107	5.625	34.21	Moderate
108	5.625	31.02	Moderate
109	7.5	54.66	Slight
110	7.5	54.65	Slight
111	9.375	55.01	None
112	9.375	55.25	Slight
113	11.25	37.21	Slight
114	11.25	41.64	Slight

* Animal died after twenty-three days.

occurred. In none of the remaining groups with 7.5 minutes' (rats 109 and 110), 9.375 minutes' (rats 111 and 112) and 11.25 minutes' (rats 113 and 114) average daily exposure, respectively, was there ever any more than a slight rachitic condition; in one case (rat 111 with 9.375 minutes' exposure) calcification was complete.

The observations from ash analysis confirm the conclusions made from the roentgenograms. According to Tisdall and Brown [21] the ash content of normal rats from 25 to 27 days of age increases in four weeks from 40 to 60 per cent, whereas that of animals fed a rachitogenic diet decreases to slightly over 30 per cent in the same length of time. The accompanying table shows the results of total ash analysis of a tibia and a femur from each of our experimental animals as well as a comparative tabulation of the roentgenographic observations. It

21. Tisdall, F. F., and Brown, A.: Seasonal Variation of Anitrachitic Effect of Sunshine, Am. J. Dis. Child. **34**:721 (Nov.) 1927.

will be seen that the results of the analysis of the ash content of the bones parallel those obtained by the roentgenographic method, and that a diagnosis of rickets made from the analysis of the ashes would agree closely with that made from the roentgenograms.

Figure 3 represents the growth curves of the experimental animals in a graphic manner. It is interesting to note that the control animals (rats 101 and 102) showed much less gain than those of any of the other groups.

COMMENT

Our experimental demonstration that exposure to direct sunlight for as little as 3.75 minutes daily has a definite antirachitic action on rats indicates that the effective biologic rays of sunlight in June and July are quantitatively of a greater magnitude in Colorado than in any of the other places where the antirachitic effect of sunlight has been studied. We believe that the relative freedom of the atmosphere from moisture and smoke offers satisfactory explanation of the comparatively high antirachitic potency of Colorado sunshine.

If this supposition is correct, one should expect a relatively low incidence of rickets in Colorado. As a matter of fact, such observations were reported by Forbes, Green and Stephenson,[22] who found an incidence of rickets in infants of 29.58 per cent by the roentgenographic method and of 27.23 per cent from clinical examination. In contrast to this, Wyman and Weymuller [23] in Boston determined that 95 per cent of all infants and 100 per cent of Italian and Negro infants have active or healed rickets before the age of 8 months. Groover, Christie and Merritt [24] in Washington, D. C., found rickets in 66.5 per cent of infants as judged by roentgenograms, and in 68.7 per cent as diagnosed clinically. Thus, the indication from these reports that infantile rickets occurs much less frequently in Colorado than in Boston or Washington supports our experimental observations that Colorado sunshine has a comparatively high antirachitic potency.

The retarded growth of the control animals, which received no exposure to sunlight, is in agreement with the observation of Fleming.[25] Two possible explanations for the failure of these animals to grow as well as the others may be offered: (1) Sunlight in itself may have a stimulating effect on growth; in its absence the control animals fail

22. Forbes, R. P.; Green, B., and Stephenson, F. B.: Arch. Pediat. **43**:131 (Feb.) 1926.

23. Wyman, E. T., and Weymuller, C. A.: Organization of Special Clinic for Treatment of Rickets with Mercury Vapor Quartz Lamp in Outpatient Department, J. A. M. A., **83**:1479 (Nov. 8) 1924.

24. Groover, T. A.; Christie, A. C., and Merritt, E. A.: Radiology **5**:189, 1925.

25. Fleming, W. D.: Mil. Surgeon **62**:592, 1928.

to make a gain proportionate to that of the other animals; (2) the control rats may have failed to grow as well as the others as a result of their marked rachitic condition. With the small number of experimental animals used, one should not attempt to draw a definite conclusion as to which of these factors is the most important. However, the data at our disposal do not support the second view. In rat 104, which was exposed for an average of 1.875 minutes daily, as marked rickets developed as in the control animals, and yet the animal gained almost twice as much in forty days (39.5 Gm. as compared with 24.5 Gm. for each of the controls). If the rachitic condition were responsible for the suppression of growth, this rat should have shown a growth curve similar to that of the controls. Thus, by elimination, we must fall back on our first assumption. Although our experimental evidence will require confirmation, there is at least an indication that sunlight in itself has a stimulating effect on growth. Certainly, our observations suggest that this subject is worthy of further investigation.

CONCLUSIONS

1. In Colorado direct sunlight in June and July has a marked antirachitic action on rats, even when the average daily exposure is as little as 3.75 minutes.

2. Only a mild degree of rickets is evident in rats exposed to direct sunlight for 7.5 minutes.

3. The high antirachitic potency of Colorado sunshine may be explained by the fact that the atmosphere is relatively free from moisture and smoke.

4. Sunshine has an apparent beneficial effect on growth. A definite explanation of this will have to await further experimental work.

A COMPARISON OF THE ANTIRACHITIC EFFECTS OF WINTER AND SUMMER SUNSHINE IN COLORADO *

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AND
HERMANN B. STEIN, M.D.
DENVER

The observation of Tisdall and Brown [1] that in Toronto a sharp increase occurs in the antirachitic effect of sunshine about the first of March aroused our interest in the question as to whether or not a similar condition exists in Colorado. The general impression which one may draw from the relatively large percentage of sunshine throughout the year, as well as from the low incidence of rickets in Colorado, suggests that there is no such marked difference in the antirachitic effect of winter and summer sunshine in Colorado as occurs in Toronto.

Forbes and Green [2] reported that from the point of view of clinical data there is a relatively low incidence of rickets in Colorado. In a continuation of this work, Forbes, Green and Stephenson,[3] by use of the x-ray method of diagnosis, confirmed this conclusion. In their reports, they gave consideration to climatologic conditions in Colorado and showed from data obtained from the United States Weather Bureau that in winter Colorado enjoys a considerably higher percentage of its possible sunshine than do Chicago, New York and New Orleans. The relatively slight variation in the percentage of total sunshine in Colorado is striking. The average monthly percentage of sunshine in Denver for thirty-five years varies only between 60 per cent (in May) and 71 per cent (in September), whereas the variation in the other cities is from 41 per cent (in December) to 73 per cent (in July). Furthermore, they called attention to the relatively low humidity in Denver (average, 53 per cent). They concluded that "the comparatively low incidence of rickets in Colorado may be attributed to the high percentage of actinic rays reaching the earth at high altitudes (about 43 per

* Submitted for publication, July 11, 1930.

* Reported before the Division of Biological Chemistry at the Columbus Meeting of the American Chemical Society, May 1, 1929.

* From the Departments of Biochemistry and Pediatrics, University of Colorado School of Medicine.

1. Tisdall, F. F., and Brown, A.: Seasonal Variation of the Antirachitic Effect of Sunshine, Am. J. Dis. Child. **34**:721 (Nov.) 1927.

2. Forbes, R. P., and Green, B.: Colorado Med. **22**:69, 1925.

3. Forbes, R. P.; Green, B., and Stephenson, F. B.: Arch. Pediat. **43**:131, 1926.

cent more at Denver than at sea level), to the higher percentage of winter sunshine and the low humidity, and to a relatively high day temperature, allowing infants to sleep out of doors in the winter months."

Several workers have reported a seasonal variation in the amount of ultraviolet light reaching the earth. Dorno,[4] using his cadmium cell method, found that at Davos, Switzerland, the ultraviolet radiations shorter than 320 millimicrons varied from winter to midsummer in the ratio of 1:11. Hill[5] reported that the acetone methylene-blue (methylthionine chloride, U. S. P.) method described by Webster, Hill and Eidinow[6] gave varying results at different places, and that there was a great loss of this radiation in smoky cities. However, in all cases the winter readings for any location were much lower than those taken in summer, varying from 1:6 at Davos, Switzerland, to 1:30 at Stirling, Scotland. Tisdall and Brown[1] found the antirachitic effect of sunshine at Toronto in April and May to be approximately eight times as great as in December, January and February. Best and Ridout[7] measured the ultraviolet radiation of the sunlight by the acetone methylene-blue method and reported a fivefold increase in Toronto from January to June. Clark,[4] using the zinc sulphide method of measuring ultraviolet radiation, showed a similar variation (a ratio of 1:8 as between winter and summer) in the intensity of solar ultraviolet radiation in Baltimore. With the same method, Earp[8] found a little less than three times as much ultraviolet radiation in August as in December in Boulder, Colo. Day[9] recently reported a marked seasonal variation in the antirachitic potency of Arkansas sunshine. He found that whereas an average daily exposure to sunshine of ten minutes over a period of forty days during June and July was sufficient to induce calcification in rats fed a rachitogenic diet, incomplete protection against rickets resulted from two and one-half hours' daily exposure to sunshine in January and February.

Comparing the intensities of ultraviolet radiations (from 290 to 350 millimicrons) found by Clark[4] and by Earp[8] in Baltimore and Boulder, respectively, one sees that in August, 1928, the number of zinc sulphide units (expressed as $1/t$, t being the time required to give

4. Dorno, C., quoted by Clark, J. H.: Am. J. Hyg. **9**:646, 1929.

5. Hill, L.: Proc. Roy. Soc. London, series B **102**:119, 1927.

6. Webster, A.; Hill, L., and Eidinow, A.: Lancet **1**:745, 1924.

7. Best, C. H., and Ridout, J. H.: Ultraviolet Radiations: Measurement by the Acetone Methylene Blue Method, Am. J. Dis. Child. **34**:719 (Nov.) 1927.

8. Earp, J. R.: Am. J. Hyg. **9**:663, 1929.

9. Day, P. L.: The Seasonal Variation in Antirachitic Potency of Arkansas Sunshine, read at the Atlanta meeting of the American Chemical Society, May, 1930.

one zinc sulphide unit) was practically the same (1.8) in both places, whereas in December the figures obtained were 0.31 (December, 1927) for Baltimore and 0.64 (December, 1928) for Boulder. Earp [10] showed a higher intensity in the shorter wave lengths (from 290 to 315 millimicrons) for Colorado even in summer. Using the difference between the zinc sulphide readings under quartz and under glass to obtain an estimate of these shorter radiations and comparing his results with those of Clark,[11] Earp showed a 59 per cent greater intensity (9,400 as compared with 5,900 ergs per square centimeter per second) in the amount of these shorter ultraviolet rays during August at Denver than at Baltimore. Comparing the January observations of these two workers, one finds Colorado sunshine (Earp [10]) in January, 1929, showing an intensity of 950 ergs per square centimeter per second as compared with 500 ergs per square centimeter per second found in Baltimore (Clark [11]) in the same month. It is interesting to note that in January, 1930, even greater differences were found (400 as compared with 2,300 ergs per square centimeter per second for Baltimore and Denver, respectively). Thus the zinc sulphide method of assay of ultraviolet light has shown from two to almost six times as much ultraviolet radiations (from 290 to 315 millimicrons) in Boulder as in Baltimore during January.

EXPERIMENTAL PROCEDURE

In order to determine whether or not the observation of Tisdall and Brown [1] that suddenly about the first of March an increase in the antirachitic effect of sunshine occurs, three groups of male albino rats were placed on the McCollum antirachitic diet 3143 (the same diet used by Tisdall and Brown and in our previous work), and the procedure of subjecting the animals to short daily exposures to direct sunshine used by us [12] the preceding summer was followed. All of the animals were carried through an experimental period of approximately forty days. The first experimental group of animals was studied for a period of forty-two days ending in the last week of February; the second, for one of forty-three days, twenty-one days in February and twenty-two days in March; and the third, for a period of forty-three days starting during the last week in February.

In each experimental group, the animals were divided into four divisions of three rats each for exposure to five, ten, fifteen and twenty minutes, respectively, of direct sunlight daily. They were not exposed

10. Earp, J. R.: Private communication to the authors.

11. Clark, J. H.: Data sent to Dr. Earp by Dr. Clark and used with the latter's permission.

12. Stein, H. B., and Lewis, R. C.: The Comparatively High Value of Colorado Sunshine in the Prevention of Rickets, Am. J. Dis. Child., this issue, p. 62.

every day, the actual number of days' exposure in the three groups being thirty-nine of forty-two days for the first group and forty-one of forty-three days for each of the second and third groups. In all cases, the exposures were made between 11 a. m. and 1 p. m. As control animals had been carefully studied the preceding year, it was not considered necessary to repeat control experiments in each group. A single control animal was carried in the third group, however. At the end of each period, the animals were killed, roentgenograms were taken, and a tibia and a femur from each animal was analyzed for its ash content.

Comparison of the Antirachitic Effects on Rats of Exposure to Sunshine at Various Seasons of the Year *

Average Daily Exposure to Sunshine, Min.		Ash of Tibia and Femur							
		Group 1 Jan. 15-Feb. 27		Group 2 Feb. 9-March 22		Group 3 Feb. 22-April 4		Group 4 June 3-July 13	
		Rat No.	Ash, %	Rat No.	Ash, %	Rat No.	Ash, %	Rat No.	Ash, %
0		....	....	.....	....	21-O	23.6†	101	18.06†
								102	24.62†
4.65 (group 1)		2-R	50.1	12-R	39.6	.....	....	107	34.2‡
4.76 (groups 2 and 3)		2-O	46.0	12-O	34.5‡	22-O	44.3	108	31.0‡
5.63 (group 4)		2-L	45.7	12-L	33.7‡	22-L	48.2		
9.31 (group 1)		3-R	48.5	.....	....	23-R	50.4	111	55.01
9.52 (groups 2 and 3)		3-O	48.5	13-O	42.9	23-O	47.2	112	33.25§
9.38 (group 4)		3-L	44.3	13-L	42.8	23-L	51.7		
13.95 (group 1)		4-R	42.0	14-R	44.7	24-R	51.6		
14.29 (groups 2 and 3)		4-O	44.5	14-O	48.4	24-O	41.7		
		4-L	45.6	14-L	48.5	24-L	46.1		
18.60 (group 1)		5-R	48.4	.....	....	25-R	48.6		
19.05 (groups 2 and 3)						25-O	57.0		
		5-L	46.2	15-L	51.6	25-L	53.3		

* There is no roentgen evidence of rickets unless otherwise noted.
† Roentgenograms show a marked degree of rickets.
‡ Roentgenograms show a moderate degree of rickets.
§ Roentgenogram shows a slight degree of rickets.

RESULTS

Table 1 gives a comparison of the results of the analyses for ash made on the tibias and femurs of the rats of the three groups, with those for the rats (group 4) studied in June and July of the previous year and reported in the preceding paper.[12] It will be seen that the control animals in groups 3 and 4 showed marked rickets, and that in none of the three experimental groups in January, February and March was there any evidence of rickets, except in those animals that were exposed for five minutes daily in the second group (from February 9 to March 22). These animals showed a marked degree of rickets. The roentgenograms, reproduction of which would add so little to the results of the analyses of the bones for their ash content that their publication is being omitted from this paper, confirm these results, just as they did in our previous report.[12]

Comparison of the ash contents of the bones of the experimental rats reported for the first time in this paper (groups 1 to 3) with those of the animals studied the preceding year (group 4) shows less protection by exposure to sunshine in June and July than in January, February and March. An explanation of this apparent anomalous result will be made in the paragraphs that follow.

COMMENT

The results obtained in the three groups of experiments here reported do not support the contention of Tisdall and Brown,[1] at least as far as Colorado is concerned, that suddenly about the first week of March there is a marked increase in the amount of biologically effective ultraviolet light reaching the earth. If this were true, the rats of group 1 would have developed marked rickets in all cases; the rats of group 2 would have shown a somewhat lesser degree of rickets on account of the protection received by them during the last half of the experimental period; and the rats of group 3 would have shown an absence of rickets. As a matter of fact, protection was as complete in group 1 as in group 3. The slightly lower protection shown in group 2 may be explained on the ground that, although the Denver atmosphere is generally relatively free from smoke, there was a definitely greater amount of smoke during the year of this experiment as a result of a coal strike that necessitated the burning of more bituminous coal than usual. Although the air in the vicinity of the School of Medicine, where the experiments were performed, was never very smoky, there was a noticeably greater amount during the experimental period of group 2 than in the experimental periods of groups 1 and 3.

The conclusion that might be made by a comparison of groups 1 to 3 (January, February and March) with group 4 (June and July), that sunshine has more antirachitic effect in winter than in summer, is discounted considerably when attention is called to certain differences in experimental procedure in the two years. In the first year (June and July experiments of group 4), the animals were exposed to sunshine at any time between 8:45 a. m. and 4:30 p. m.; whereas in the January, February and March experiments of groups 1 to 3 performed the following year, the exposures were always made between 11 a. m. and 1 p. m. Clark [4] and Earp [5] reported a marked variation in the amount of ultraviolet light during the different hours of the day, with the maximum occurring during the middle of the day. Our failure to expose our rats of the June and July experiments (group 4) during this period of maximum ultraviolet light is undoubtedly responsible for the lesser protection found by us in summer than in winter.

Furthermore, the rats of our summer experiment (group 4) were exposed on from 75 to 78 per cent of the experimental days, whereas

the animals of our winter experiment (groups 1 to 3) were exposed on from 93 to 95 per cent of the days of the experimental period. That this difference in experimental method was partly responsible for the lesser protection of the summer group is altogether probable.

Consequently, one should not draw definite conclusions from our experiments about the comparative quantitative antirachitic value of winter and summer sunshine.

However, it is evident from our experimental data that winter sunshine in Colorado contains a high concentration of biologically effective ultraviolet light. This is in entire agreement with the observations of Earp,[10] who has shown that the intensity of short wave radiations (from 290 to 315 millimicrons) may remain at a relatively high level (above 2,000 ergs per square centimeter per second) throughout the winter in Colorado.

Furthermore, taking into consideration the differences in experimental technic mentioned, we believe that our data demonstrate that there is no marked difference in the antirachitic effect of winter and summer sunshine. Earp[8] showed that the variation in short wave lengths between 9 a. m. and 3 p. m. in July is only 25 per cent of the minimum found at the beginning and at the end of the period, there being a gradual rise to a maximum at 11 a. m., which continues until 1 p. m., and is followed by a gradual fall to the minimum again at 3 p. m. As most of our animals were exposed to sunshine between 9 a. m. and 3 p. m., the protection that we have found for June and July was probably not considerably less than it would have been, had we exposed these animals to sunshine between the hours of 11 a. m. and 1 p. m.; and yet sufficiently great to account for the lesser protection in June and July.

If there is a variation in the amount of short wave lengths between winter and summer sunshine in Colorado, as has been shown by Earp[13] by the zinc sulphide method, how can we account for the fact that we have found no demonstrably lesser protection by sunlight in winter than in summer? We might argue that the chemical method is not as true a criterion of the amount of biologically active ultraviolet light as is the method of animal experimentation, but we feel that such an argument can be neither proved nor disproved by available data. A better explanation would seem to be that for protection against rickets rats need a certain minimum amount of short wave length energy, that winter sunshine in Colorado contains at least this minimum amount, and that no greater protection is rendered by the somewhat greater amount found in summer sunshine. Such a theory would be in entire accord with

13. Earp (footnotes 8 and 10).

present knowledge concerning the effect of any excess of vitamins above the minimum requirement.

CONCLUSIONS

1. Winter sunshine in Colorado contains a high concentration of biologically effective ultraviolet light.

2. Our experimental results do not support the contention of Tisdall and Brown, at least as far as Colorado is concerned, that suddenly about the first of March there is a marked increase in the amount of ultraviolet radiations reaching the earth.

3. There is no marked difference in the antirachitic effect of winter and summer sunshine in Colorado.

4. The comparatively high antirachitic action of Colorado sunshine with relatively little seasonal variation as compared with that of other places where similar studies have been made may be explained on the ground that throughout the year relatively short wave radiations reach the earth as a result of (1) the high percentage of winter sunshine, (2) the low humidity and (3) the small amount of smoke in the atmosphere.

PERICARDITIS WITH EFFUSION *

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The object of this paper is to call attention to the pulmonary signs associated with moderate and large pericardial effusions. Although Pins,[1] in 1889, described these signs in "A New Symptom of Pericarditis," and Curschmann,[2] in 1907, wrote a classic article demonstrating the anatomic reasons for their occurrence, it has not been generally recognized that the effusion itself is responsible for the production of striking physical signs in the lower part of the chest posteriorly. In 1926, Conner [3] called attention to the work of previous investigators and presented his views of the clinical and anatomic considerations of pericardial effusion.

For many years the pulmonary signs found in children with rheumatic heart disease at Bellevue Hospital were discussed, and various diagnoses—usually of compression of the lung, pneumonia, pleural effusion or pulmonary infarction—made. It is now believed that pericardial effusion is the correct interpretation of the signs that I shall describe.

In considering the diagnosis of pericardial effusion, two facts must be kept in mind: 1. Contrary to earlier teaching, the heart does not change its position materially in the presence of effusion. The attachments are so firm, and the heart so completely fills the space between the anterior wall of the chest and the spinal column, that it is impossible for it to sink downward and backward as was formerly assumed to be the case. Curschmann and others showed clearly that in the presence of effusion, the heart, except possibly the apex, maintains its position in relation to the anterior wall of the chest. 2. An inflamed pericardial sac is distensible far beyond the capacity of a normal pericardium.

Because of the attachments of the great vessels, and the fact that the heart lies a little more to the left than to the right side of the chest, the left pouch of the pericardium becomes more distended with fluid than

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1. Pins: A New Symptom of Pericarditis, Wien. med. Wchnschr. **34**:209, 1889.

2. Curschmann, H.: Deutsche Klinik **15**:401, 1907.

3. Conner, L. A.: On the Diagnosis of Pericardial Effusion, Am. Heart J. **1**:421 (April) 1926.

does the right. As it becomes more and more filled, it extends posteriorly below the hilus of the lung, pushing the lung upward and laterally, until the pericardium actually comes in contact with the posterior wall of the chest. Curschmann thought that the lung was pushed medially against the vertebral column, but I agree with Conner that it must be compressed laterally (fig. 1). The signs thus produced range from dulness to flatness on the left side of the chest from the angle of the scapula down. Over all or part of this area there is bronchial breathing, usually intense, with bronchophony or egophony. A similar but smaller area is often present on the right side of the chest. The bronchial voice and breathing are produced by the transmission of the sound directly

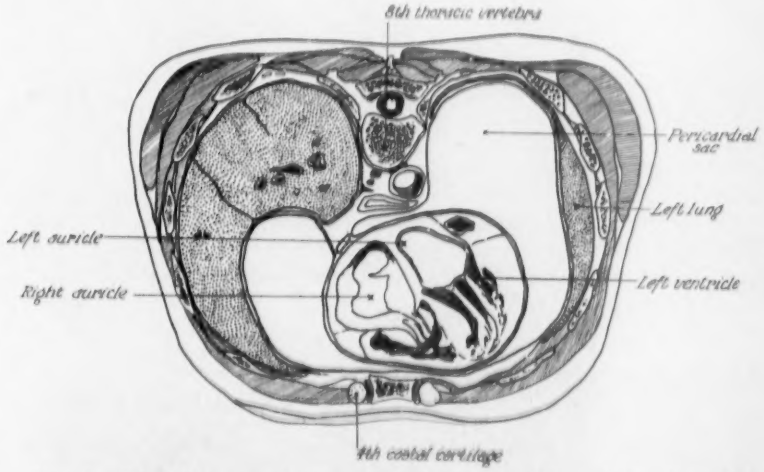

Fig. 1.—Semidiagrammatic illustration of the position of the distended pericardium in relation to the heart, the lung and the wall of the chest. (Diagram based on section from "Manual of Surgical Anatomy" published by the Medical Department of the United States Army and Navy, and illustration from Conner: Am. Heart J. 1:421 [April] 1926).

from the bronchus through the pericardial fluid. When the fluid is just beginning to accumulate and the amount is still small, an area of slight dulness may be found just inside the angle of the left scapula, with breath sounds which are harsh or faintly bronchial.

Tactile fremitus persists, but may be diminished. Frequently there are fine râles just above the area of dulness and bronchial breathing. I have found, as Conner did, that there is always an area of resonance, sometimes very small, between the dulness of the posterior side and that of the left border of the heart. The outline of the area over which these signs are found is distinctive in contrast to that found in pleural effusion (figs. 2, 4, 8 and 12). In pericardial effusion, the area is

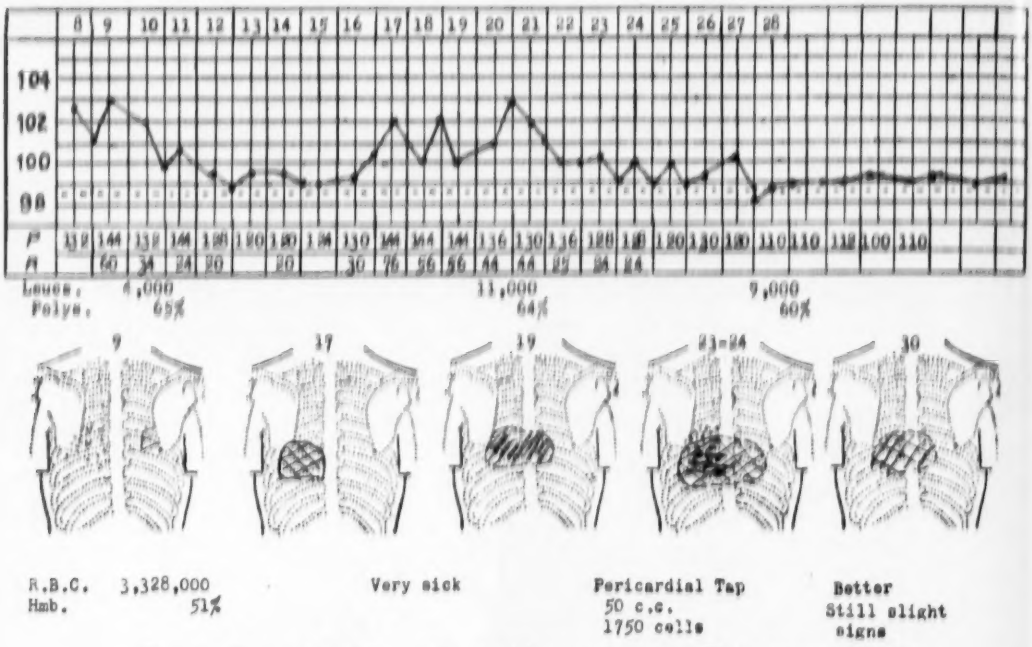

Fig. 2.—Chart of A. M., a colored girl, aged 9 years. There was no history of rheumatic fever; however, she had had col[illegible] for the past two years, "neuritis" with pain in the legs six weeks previous to admission and pain in the back, headache, cough when in a supine position, fever and night sweats five days before admission to the hospital. Examination of the heart revealed a double mitral lesion and friction rub.

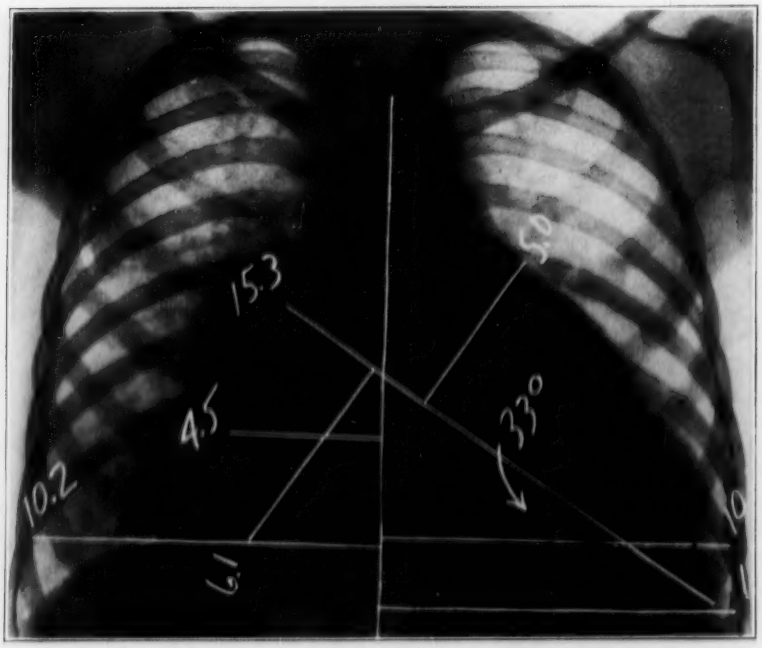

Fig. 3.—Roentgenogram of A. M., taken the day before the pericardial tap. Signs were present as indicated in figure 2. There was no roentgen evidence, however, of pleural effusion.

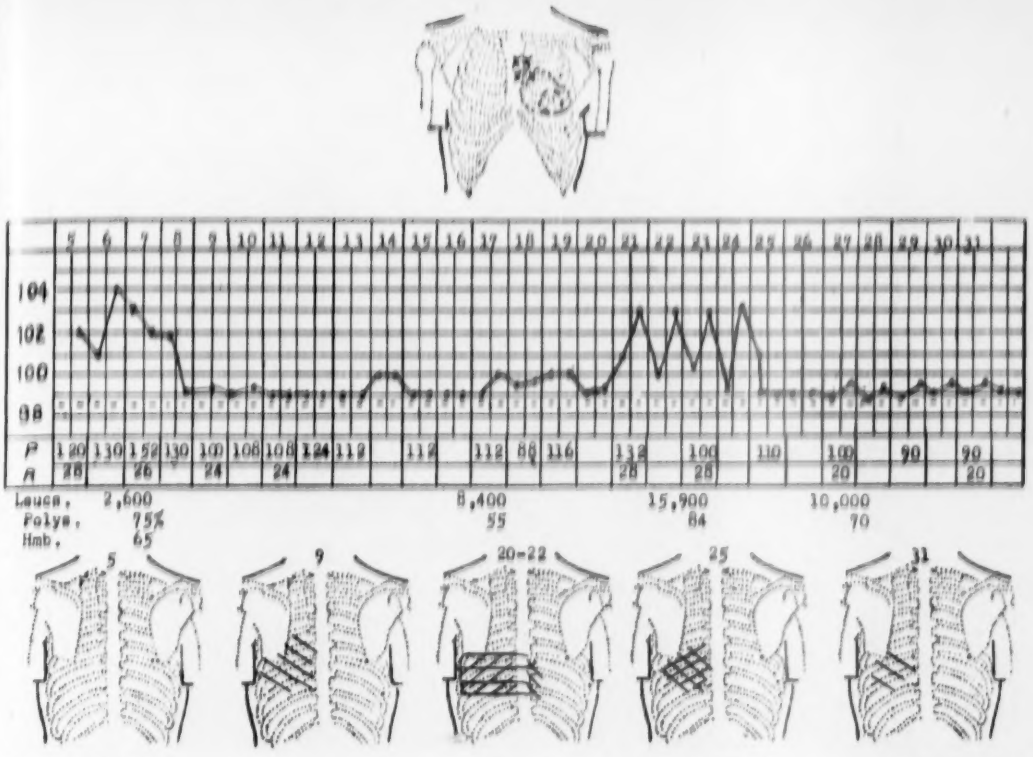

Fig. 4.—Chart of P. J., aged 6 years, under observation from Oct. 5, 1929, showing development of pulmonary signs. There was no history of rheumatic fever. The illness had commenced one day before admission to the hospital with fever and pain in the foot and the upper part of the abdomen. On examination, the heart showed a definite systolic murmur, a slight diastolic murmur and friction rub; the lungs were clear.

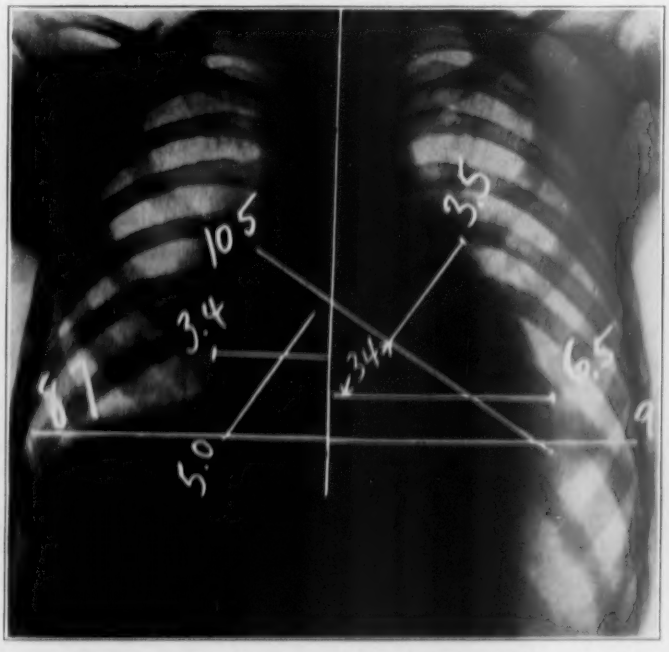

Fig. 5.—Roentgenogram of P. J., taken at time of admission. There are no signs of pericardial effusion.

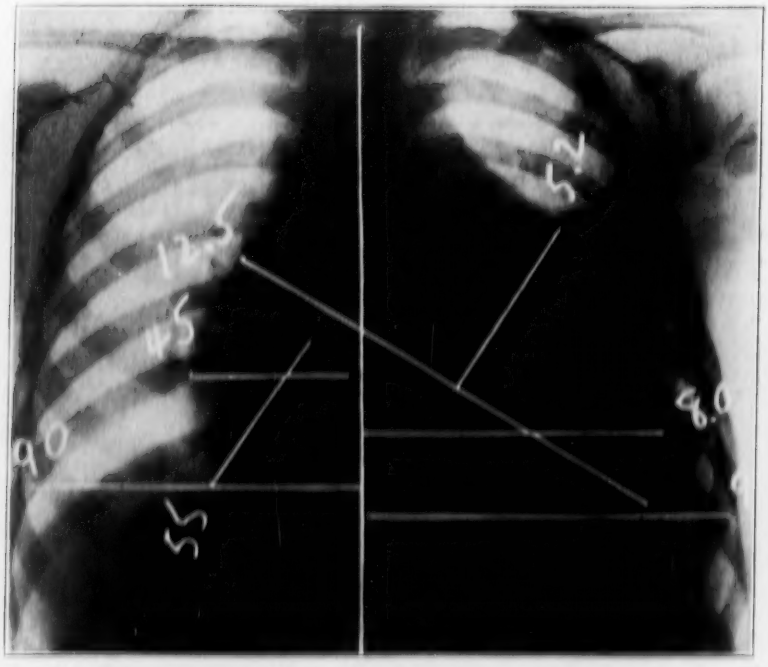

Fig. 6.—Roentgenogram of P. J., taken nine days after admission. There are some signs of pericardial effusion, and some pulmonary signs.

Fig. 7.—Roentgenogram of P. J., taken immediately after tap. There is no evidence of pleural effusion. Note the pneumothorax on the left.

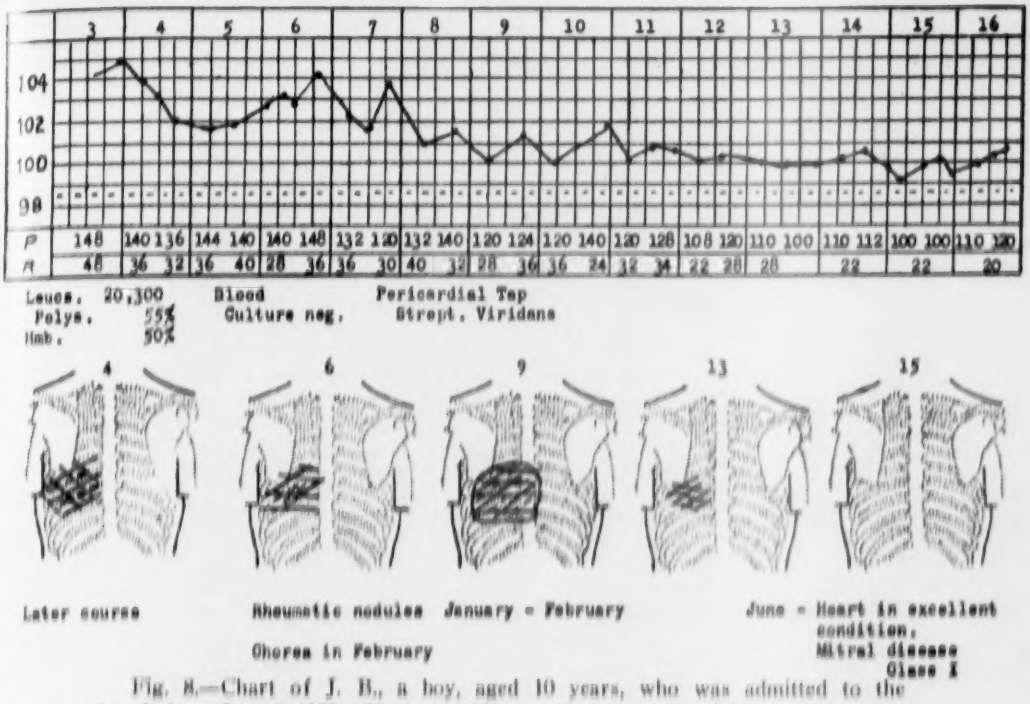

Fig. 8.—Chart of J. B., a boy, aged 10 years, who was admitted to the hospital on Jan. 4, 1930. He had a history of chorea from 1927 to 1929, and a tonsillectomy in May, 1929. He was ill with dyspnea, fever and pain in the ankle, knee and chest for two weeks previous to admission. Examination of the heart revealed a friction rub over the entire precordium and a double mitral lesion.

Fig. 9.—Roentgenogram of J. B., taken on admission, the day of the pericardial tap. There was no evidence of pleural fluid. Note the characteristic shadow of the pericardial fluid.

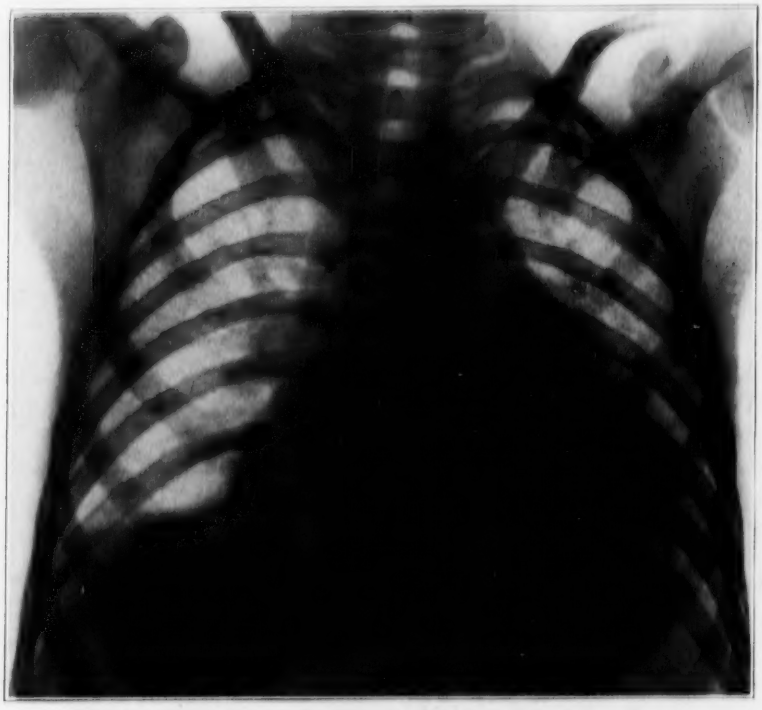

Fig. 10.—Roentgenogram of J. B., taken eighteen days after figure 9. There is possibly a small amount of pericardial fluid still present; there are no pulmonary signs.

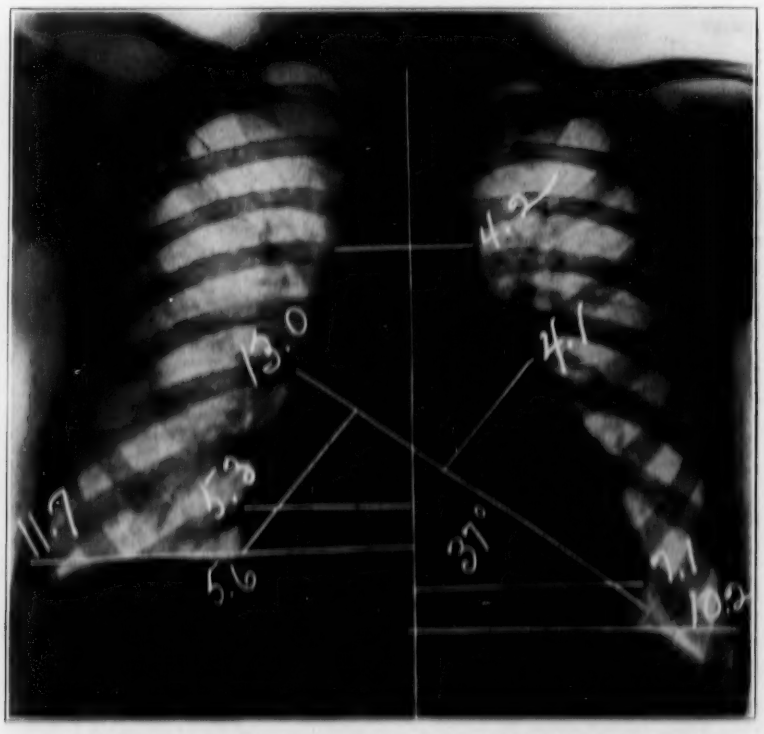

Fig. 11.—Roentgenogram of J. B., taken six weeks after the tap. There are no signs in the lung nor pericardial fluid.

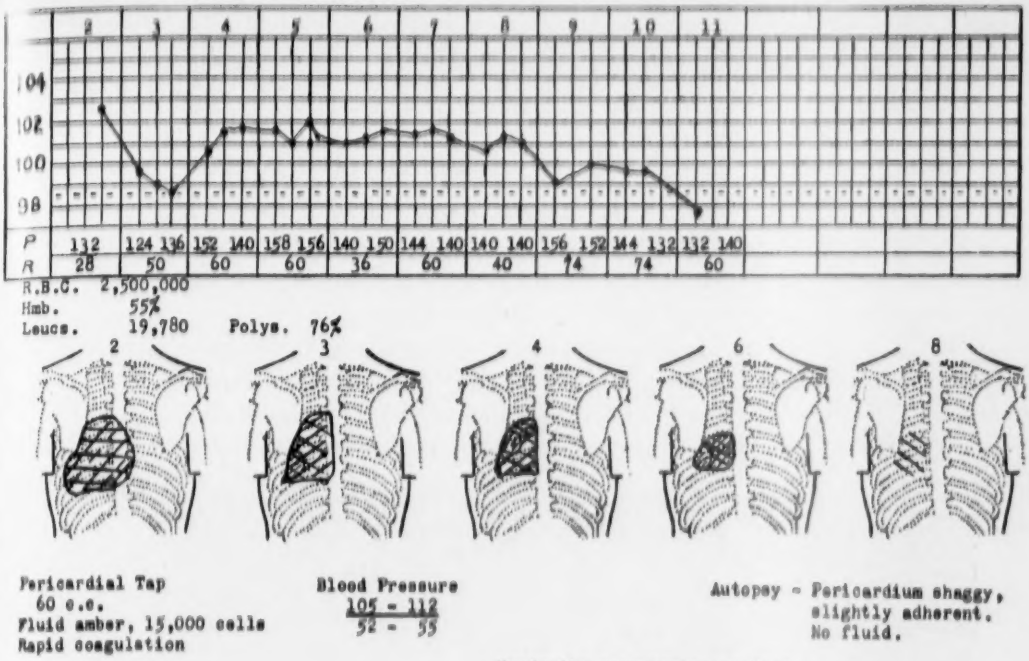
2 3 4 5 6 7 8 9 10 11
104
102
100
98
P 132 124 136 152 140 158 156 140 150 144 140 140 140 156 152 144 132 132 140
R 28 50 60 60 36 60 40 74 74 60
R.B.C. 2,500,000
Hmb. 55%
Leucs. 19,780 Polys. 76%
2 3 4 6 8
Pericardial Tap
60 c.c.
Fluid amber, 15,000 cells
Rapid coagulation
Blood Pressure
105 - 112
52 - 55
Autopsy - Pericardium shaggy, slightly adherent. No fluid.
Gradually grew worse and died.

Fig. 12.—Chart of R. B., a girl, aged 8 years, under observation from May 2 until death on May 11, 1930. There was no history of rheumatic fever. The onset of the illness was sudden, with vomiting, pain in the neck and dyspnea. She was sent to the Willard Parker Hospital with a diagnosis of meningitis, but a spinal tap gave negative results. The child, at the time of examination, was extremely ill and suffered from extreme dyspnea. The heart revealed signs of a friction rub, muffled sounds, a double mitral murmur and a range in heart rate from 150 to 160. There were also signs at the base of the left lung.

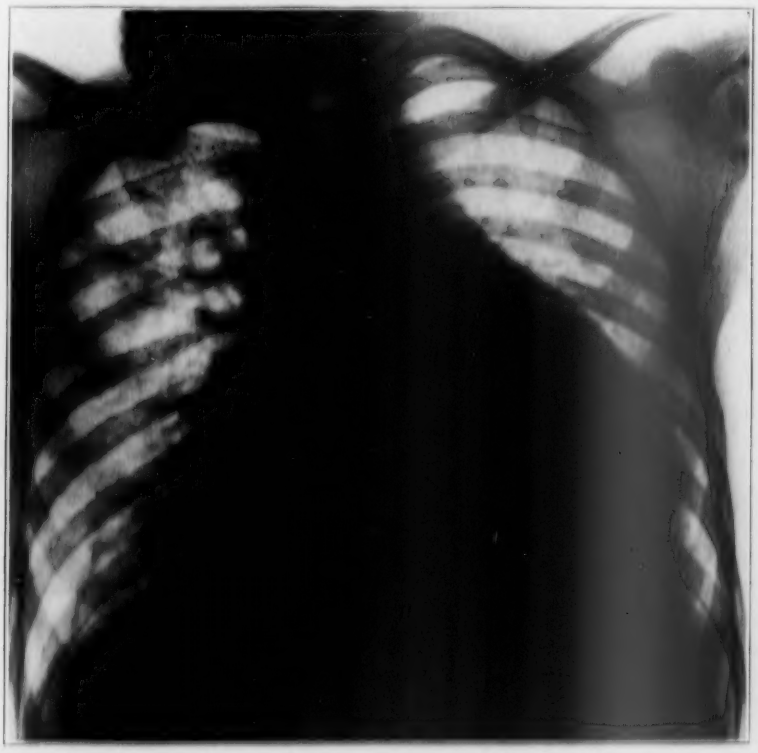

Fig. 13.—Roentgenogram of R. B., taken on admission, the day of the pericardial tap. There is no evidence of pleural fluid. Note the characteristic shadow of the pericardial fluid.

round or square, and the outer margin falls off sharply, while in pleural effusion the upper limit of the signs is the classic Ellis line, which is lower at the spine than in the midscapular line, and which slopes off gradually toward the axilla. These signs disappear gradually with the absorption of the fluid, which is usually complete in from ten to fourteen days (fig. 11).

In order to demonstrate that these signs actually are produced by the pericardial fluid, eight cases have been studied carefully, and have

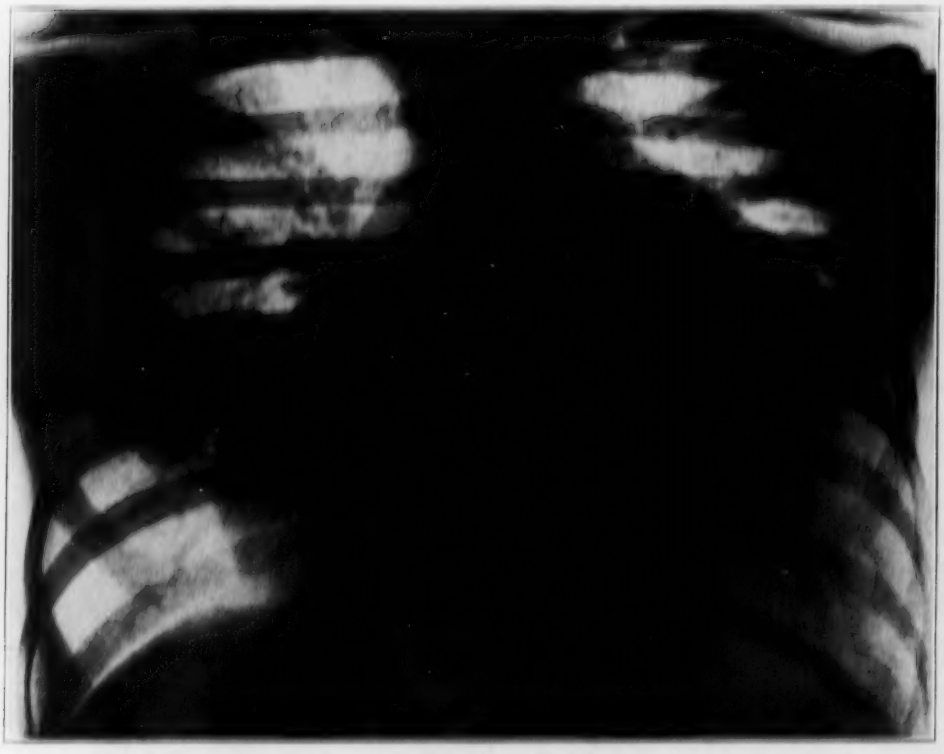

Fig. 14.—Roentgenogram of R. H. There is evidence of a large amount of pericardium effusion. Intense pulmonary signs were present on both sides of the chest posteriorly. Only a large amount of pleural fluid could have given such extensive signs, and there was no roentgen evidence to indicate this. The pericardium was tapped twice posteriorly and about 200 cc. of fluid was withdrawn each time. (After Sutton and Smith: Heart Disease in Infancy and Childhood, New York, D. Appleton & Company, 1930.)

proved satisfactorily that Curschmann's explanation is in the main correct. Every case has shown roentgen shadow characteristic of pericardial effusion; the pulmonary fields, as shown by roentgenograms or by fluoroscopy, have been clear, thus excluding the presence of pleural

fluid (figs. 3, 6, 7, 9, 10, 13 and 14; for contrast see fig. 15), and fluid has been easily obtained by thoracentesis in the seventh or eighth space posteriorly.

It is not necessary here to go into the other physical signs of pericardial effusion. It is interesting to note that the pericardial friction rub was heard in all cases while effusion was known to be present. In some patients it became less pronounced, and in two patients it was not audible for a day or two, but was heard most of the time. The persistence of the rub, therefore, does not exclude the presence of effusion.

Fig. 15.—Roentgenogram of J. H. There were signs of rheumatic pleurisy with effusion. Compare this figure with the other illustrations. The shadow disappeared after thoracentesis. Later, a roentgenogram indicated a small amount of pericardial fluid, but no pulmonary signs appeared. (After Sutton and Smith: Heart Disease in Infancy and Childhood, New York, D. Appleton & Company, 1930.)

In the second case, in which a tap was made, posteriorly, before the position of the lung was determined, the needle was inserted more laterally than in any other case. This produced a pneumothorax with almost complete collapse of the lung (fig. 7). This caused the child no discomfort, and the air was rapidly absorbed. Since then a site about the center of the flattest area, usually nearer the spine than the axilla, has

been chosen, and in no other case has the lung been pierced. One child came to autopsy nine days after the tap (fig. 12), and there was no evidence on the visceral pleura of puncture by the needle.

COMMENT

The signs described, developing in a child with rheumatic fibrinous pericarditis, constitute in themselves evidence of the presence of pericardial effusion. If any doubt exists, fluoroscopy or an x-ray picture will clear it up. The posterior site for tapping the pericardium is perfectly safe, and one is far more certain of reaching the fluid than in using the points formerly recommended. Although only one of my cases seemed to require relief because of the size of the effusion, it appears possible that removal of some of the fluid may hasten absorption and thus lead to quicker recovery. One certainly need have no hesitation in adopting this procedure either for diagnostic or for therapeutic purposes.

Dr. Charles Hendee Smith assisted me in mapping out the signs and in making the charts.

Case Reports

MEDIASTINAL TERATOMA IN AN INFANT*

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AND
MARTHA WOLLSTEIN, M.D.
NEW YORK

Mediastinal tumors in young children are not common, and solid teratomas in the thoracic cavity are especially rare. The following case is reported because of its clinical and pathologic interest.

REPORT OF CASE

History.—The patient was first seen at the age of 6 months, at which time there was no suspicion on the part of the parents of any serious disease. He was an only child, of normal birth. The family history was negative as to any constitutional disease. He had not been seen by a physician since his mother was dismissed by her obstetrician. The weight was 18½ pounds (8,391 Gm.).

Although the parents said that the patient had always been free from symptoms of any sort, on closer examination it developed that for the past three months, since the age of 3 months, there had been periods in which the respiration seemed hurried and the child slightly uncomfortable. Other than this, the progress of digestion, growth and development had been normal.

About one week previous to the first observation, the respiratory difficulty had become more marked. After two days, however, the patient seemed so much improved that he was taken out and his normal regimen was resumed. The following day, dyspnea developed, with hurried and labored respirations, sleeplessness and general discomfort. This was, however, not severe enough to interfere with his taking food normally. An opinion was asked concerning the child, largely because of the fear that some acute contagious disease might be developing, not because there was any suspicion of serious illness.

Examination.—On examination, the patient appeared relatively comfortable; the respirations, numbering about 40, were hurried and shallow; the color was good and the pulse rate, 120, was of good character. He was well nourished. The neck seemed short and thick, and the shoulders high. Superficial examination revealed nothing else. There were no disturbances of the superficial circulation.

The right side of the chest appeared more prominent than the left, particularly in its upper anterior aspect, and measured from sternum to spine 4 cm. more than the left side at the same level. Percussion revealed absolute flatness anteriorly and in the axilla from the clavicle to the line of the liver. Posteriorly, there was

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* From the Babies' Hospital and the Pediatric Department of Columbia University, College of Physicians and Surgeons.

a moderately impaired resonance. The breath sounds anteriorly and in the axilla were bronchial or amphoric, with diminished intensity. The left side of the chest was moderately hyperresonant. The apex of the heart was not palpated. There seemed to be a displacement of the heart to the right. Examination of the abdomen gave negative results. The temperature was 101.5 F.

The diagnosis at this time seemed to rest between a new growth of the lung or the mediastinum and fluid in the pleural sac.

Course.—The condition was explained to the parents, and roentgenogram and further examination requested, but nothing more was heard from them for one week, at which time the infant was brought to the hospital in collapse, with a temperature of 105 F. His condition was so unfavorable that a detailed examination was omitted, except for the making of a hurried roentgenogram, which showed the right side of the chest to be occupied in its entirety by a mass of considerable density. The infant was placed in an oxygen tent, where for about two hours he showed some evidences of relief from the dyspnea and improvement in the character of the pulse.

At this time a needle was inserted in the right axillary line in the fifth space; 135 cc. of bloody fluid was removed, which proved to be sterile.

The condition grew steadily worse, and at the end of another hour the child died, with a temperature of 110 F.

Examination of the blood showed: hemoglobin, 86 per cent; red blood cells, 4,920,000; white blood cells, 23,000, and polymorphonuclears, 67 per cent.

Chemical analysis of the blood showed: nonprotein nitrogen, 60; chlorides, 650; sugar, 136; albumin, 1.9, and globulin, 1.9.

Clinically, the picture was that of a child aged 6 months, well nourished and, on superficial examination, normal, except for respiratory embarrassment, which had existed for one week before death. The history was one of normalcy up to 3 months of age, when symptoms of respiratory difficulty appeared, so mild, however, as to cause no concern on the part of his attendants.

Autopsy.—A complete autopsy was refused, but permission to do a thoracotomy was obtained. A portion of the sixth, seventh and eighth ribs on the right side was removed, and the thoracic contents viewed through the opening. There was a gray, dry exudate over the right parietal and visceral pleura, and also over the upper surface of the right half of the diaphragm. The right lung was thin, compressed, dark red and pushed against the wall of the chest by a globular mass, 7 by 7.5 cm. in diameter, which occupied most of the right side of the thoracic cavity. It was closely attached to the thymus by adhesions which were readily torn. The heart was pushed to the left, and was quite free from the tumor.

The left lung was aerated. Its upper lobe was pink, while the lower lobe was deeply congested and bluish red. No fluid was present in the left pleural cavity. The heart was triangular and of normal size. The vessels and valves were normal. The ductus arteriosus and foramen ovale were closed. The thymus gland weighed 16 Gm. It was congested, and its capsule was adherent to the capsule of the tumor, from which it was easily separated. The other organs were normal.

The tumor weighed 138 Gm., had a smooth red capsule and did not fluctuate. On incision no fluid escaped. It was composed of four lobules and about twelve smaller ones. All of these lobules were solid and covered by pink, embryonal skin with lanugo hairs. Adherent to the skin was a thin layer of grayish vernix. The four large lobules were so arranged as to suggest thighs and upper arms (fig. 1). Between the larger pair there was a depression suggestive of female

Fig. 1.—Tumor with capsule opened, showing the conformation of the four large lobes and numerous small nodules.

Fig. 2.—Skin covering the tumor, showing hair follicles and sweat and sebaceous glands.

genitalia. Numerous small lobules, all covered by pink skin, varied from 2 mm. to 1 cm. in length. On section, the masses showed yellow, lobulated fat, with long pieces of cartilage in some and red, soft, apparently undifferentiated tissue. Along the posterior border the capsule was firmly adherent and incision showed the presence of a cavity 0.5 by 0.5 cm., in diameter, lined by a smooth, glistening membrane and containing a few drops of turbid fluid in which fat was found. At the upper pole a globular nodule was softer than the rest, with an even, cut surface. The inner surface of the capsule was irregular, folded and vascular, but no large vessels were seen to penetrate it from the outside.

A roentgenogram of the tumor after its removal demonstrated the presence of small areas of cartilage, but none of bone.

Microscopic Examination.—On microscopic examination, the right lung showed intense congestion, edema, thrombi in several veins and some atelectasis. The pleura was edematous with hemorrhage into its substance and granular fibrin on the free surface. The liver showed congestion and moderate fatty infiltration. The spleen and the kidneys were congested. The thymus was normal, but its capsule was congested and edematous and adherent to a layer of connective tissue into which hemorrhage had occurred, and which was continuous with the tumor capsule. Sections were taken from all of the large lobes and from most of the smaller lobes of the mass. In every case there was a covering of skin (fig. 2). The epidermis showed various degrees of desquamation over a normal rete and a congested corium. In most places the papillae were flat and not well formed. Many normal hair follicles and sebaceous and sweat glands were present. Some of the hairs were pigmented. Around the hair follicles were many bundles of unstriped muscle. The cross-section of a loop of the large intestine had goblet cells in the glands (fig. 3), a narrow submucosa and two layers of unstriped muscle with lymph nodes between the glands. Its wide lumen was filled with a pink-staining, granular material. There was much dense, fibrous connective tissue close to the intestine, and in it were congested blood vessels and several nerve trunks cut longitudinally and obliquely. In another section, there were several large masses of cartilage, two of which were arranged end to end like the long bones of an extremity. There was also a round piece of cartilage covered with a mucous membrane containing mucous glands and lined with several layers of tall epithelium, the uppermost showing cilia (fig. 4), so that the structure suggested a cross-section of the trachea. Again there was a tube of unstriped muscle lined with many layers of flattened epithelial cells. This squamous epithelium merged into a single layer of tall cells covering a mucous membrane in which were glands resembling those of the pylorus. Here were apparently the esophagus and the stomach. Myocardium with many vacuolated cells appeared, and tubules which might have been bronchioles. There were also lobules of lymphoid tissue with small Hassall's bodies, the thymus gland being an integral part of the tumor and not of the thymus of the patient. A section from the nodule at the upper pole of the tumor showed four vesicles lined with tall columnar epithelium, but the walls did not have the structure of cerebral vesicles or ventricles. Close by lay a tangled mass of medullated nerve fibers with many blood vessels among them. In another section, was a cross-section of the fallopian tube. Mucous and serous acini were arranged in lobules, as they are in a salivary gland. Small lymph nodes were scattered through many of the sections, and a thick-walled structure of unstriped muscle, lined with columnar epithelium suggested the uterus (fig. 5) continuous with a vagina lined by stratified, squamous epithelium. A small area of striated muscle was found, but no bone appeared in any of the sections. A portion of the liver, with comparatively large sinusoids was present.

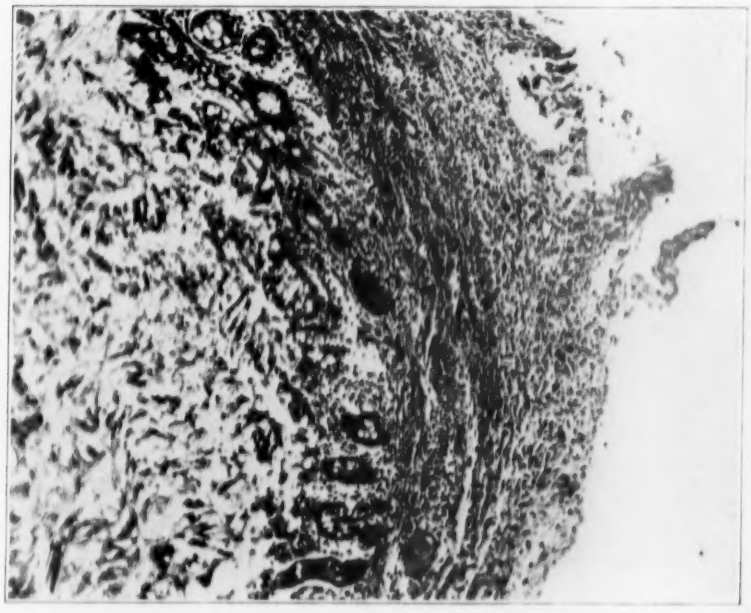

Fig. 3.—Cross-section of colon, showing lumen filled with granular débris and goblet cells in the glands.

Fig. 4.—Ciliated cells lining the trachea.

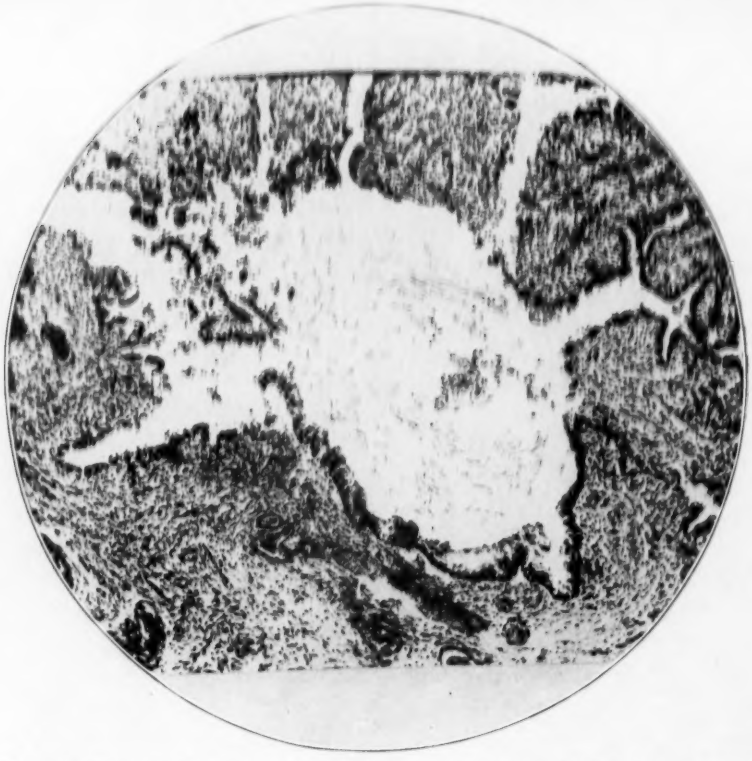

Fig. 5.—Thick-walled tube of unstriped muscle with epithelial lining suggesting the uterus and folds of the cervix.

Fig. 6.—The lining of the capsule over the tumor.

The capsule of the tumor was covered with a layer of flattened cells and was made of fibrous connective tissue lined with a layer of more delicate connective tissue in which were many fibroblasts. This thinner layer carried blood vessels from which hemorrhage had occurred. Some low villous-like projections were present (fig. 6) and were probably the rugae seen in the gross specimen. A lobule of the infant's thymus was adherent to one part of the capsule.

COMMENT

It is apparent that the tumor contained elements from all three embryonal layers. From the ectoderm came the epidermis, the hairs, the sweat and sebaceous glands and the nerve trunks; from the mesoderm came the connective tissue, cartilage, striped and unstriped muscle, myocardium and lymph nodes, and from the entoderm came the lining of the esophagus, stomach, colon, trachea and the liver. Thus the tumor was a solid teratoma, the rarer type of neoplasm found in the anterior mediastinum, in which dermoid cysts and teratomas, either cystic or solid, occur.

In 1924, Smith and Stone [1] reviewed the literature on tumors of the mediastinum in children, and reported two cases. They found only ten instances of mediastinal teratomas or dermoids in children, aged 12 years or less, including the one they reported. Five of the ten were dermoid cysts, and five were teratomas, all but one of which, reported by Pohl,[2] were cystic. Since 1924, Grimm [3] reported briefly a fluctuating tumor in the anterior mediastinum of an infant, aged 3 months, the diagnosis having been made on roentgen examination and confirmed at autopsy. Poynton's [3a] case was that of an infant, aged 4 months, with a teratoma in the mediastinum from which he died when 9 months old. Bull [4] detailed the history of a girl, aged 8 years, who recovered after the removal of a dermoid cyst from the anterior mediastinum. Bussi's [5] patient was a boy, aged 13 years, who died after the operative removal of a teratoid tumor. The other cases reported since 1924 occurred in adults. There are only fourteen cases, including the one here reported, of such tumors in children of 12 years or less,

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4. Bull, P.: Mediastinal Dermoid and Teratoid Tumors, Norsk mag. f. laegevidensk. **90**:329, 1929.

5. Bussi, A.: Di un tumore teratoide nel cavo toracico, Policlinico (sez. prat.) **34**:169, 1927.

and only eight cases in children under 5 years. Tumors occurred in girls more frequently than in boys in this group. The only tumors in infants included in the series were one reported by Medoei,[6] which was a dermoid cyst, that of Grimm,[6] which was a cystic teratoma, Poynton's teratoma and the one reported here, which was a solid teratoma. Williams [7] mentioned Zipkin's case of a stillborn fetus, but I was unable to find the report. Among the fourteen cases, six were dermoid cysts, and eight were teratomas, of which four were cystic and four were solid. One of the cystic teratomas reported by von Eiselberg,[8] became a malignant sarcoma. Von Török [9] described a tumor covered by skin, as was the one reported here. In consequence of this, of the adherent vernix and of the conformation of the mass, a parasitic fetus was suggested. Von Török's case, in which there were a head with hair and loops of a well developed intestine, was such a parasitic fetus. The cross-section in our case did not show any gross organs that could be identified, so the diagnosis of parasitic fetus was not borne out. Microscopically, the picture was that of an irregular mixture of abortive attempts at the formation of many viscera, with the greatest success attained in the case of the stomach, colon, uterus, fallopian tube, thymus gland and skin. The heart and liver were most rudimentary, while part of the respiratory system (trachea) was recognizable.

The success of operative removal is demonstrated by Madelung's [10] patient, aged 12 years, from whom a tumor was removed, after she had been under observation since the age of 6. The first symptoms (pain and hemothorax) followed a fall. One year later pleuritis developed after a cold, and during the next three years, four operations for resection of a rib were performed, because the diagnosis was empyema which refused to heal. Finally, in an attempt to cure the sinus, the tumor was removed, and the child recovered. At the age of 16 she was healthy.

The origin of teratomas is the most interesting part of the problem. It is plain that only a totipotent cell can give origin to tissues from all three germinal layers. This may be an aberrant sex cell, the undoubted origin of teratomas of the sex glands, and, possibly, the source of thoracic or abdominal teratomas, since "the possibility of strayed genital cells must be admitted and these strayed cells may perhaps form the

6. Medoei: Budapester Brief, Berl. klin. Wchnschr. **39**:719, 1902.
7. Williams, W. R.: Tumors of the Thorax, M. J. & Rec. **125**:6, 1927.
8. Von Eiselberg: Zur Therapie der Dermoide des Mediastinum Anticum, Arch. f. klin. Chir. **71**:575, 1903.
9. Von Török, G.: Teratom der Brusthohle, Ztschr. f. Heilk. **21**:263, 1900.
10. Madelung, O. W.: Ueber Extirpation eines Dermoides des Mediastinum Anticum, Beitr. z. klin. Chir. **41**:217, 1903.

parent cells for tumors and especially for teratomas."[11] A displaced blastomere, though it has never been observed or proved, may theoretically give rise to a teratoma if it has been isolated at a sufficiently early stage of its potency. Finally, a bud from the early blastoderm before the three layers have definitely separated may conceivably originate a teratoma.

As Stone and Smith[1] pointed out, the small number of these cases in young children compared with those in young adults and older persons is striking. The proportion is roughly about one to ten. The symptoms in our patient, as in others, were those of respiratory difficulty, the bulging of one side of the chest, the presence of blood-stained fluid in the pleural cavity and an x-ray picture of a large area of density greater than could be accounted for by the fluid. In Stone and Smith's case the last fluid examined contained a few hairs, which is a common observation in mediastinal dermoids. The treatment can only be surgical.

SUMMARY

A case of solid mediastinal teratoma occurring in a male infant of 6 months, giving symptoms over a period of three months, together with the microscopic content of tissues from the three embryonal layers, is detailed.

11. Keibel and Mall: Human Embryology, Philadelphia, J. B. Lippincott Company, 1912, vol. 2.

SUBACUTE BACTERIAL ENDARTERITIS OF PULMONARY ARTERY ASSOCIATED WITH PATENT DUCTUS ARTERIOSUS AND PULMONIC STENOSIS *

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Congenital defects of the heart or arteries and valvular malformations predispose to acute bacterial inflammatory processes. It is well known that an area of fibrosis resulting either from a congenital anomaly or from a healed rheumatic infection may become the site of a subsequent bacterial inflammation. Many observers have pointed out the importance of mechanical strain resulting from the impingement of anomalous currents on the endocardium in producing foci susceptible to bacterial implantation. The numerous instances reported in the literature that have been collected and analyzed by Abbott [1] support such a relationship.

In the present communication we wish to report an instance of subacute bacterial endarteritis (*streptococcus viridans*) of the pulmonary artery and ductus arteriosus associated with patent ductus arteriosus and pulmonic stenosis, in which the valves showed no inflammatory changes. This, to our knowledge, is the first instance on record of the association of pulmonic stenosis with patent ductus arteriosus in the absence of septal defect. This is the fifth instance of patent ductus on record to our knowledge in which the bacterial infection was limited to the pulmonary artery and spared the valves. Schlaepfer [2] and Krzyzskowski [3] described instances in which the process was confined to that portion of the pulmonary artery near the ductless opening. Philpott [4] reported an instance of patent ductus with vegetative endarteritis

* Submitted for publication, April 28, 1930.

* From the Division of Laboratories, Montefiore Hospital.

1. Abbott: Inflammatory Processes in Cardiovascular Defects, Ann. Clin. Med. **4**:189, 1925; Congenital Heart Disease, in Osler and McCrae: Modern Medicine, Philadelphia, Lea & Febiger, 1927, vol. IV.

2. Schlaepfer, K.: Chronic and Acute Arteritis of the Pulmonary Artery and of the Patent Ductus Arteriosus, Arch. Int. Med. **37**:473 (April) 1926.

3. Krzyzskowski: Aneurysma des Stammes der pulmonal Arterie bei Persistenz des Ductus botalli, Wien. klin. Wchnschr. **4**:92, 1902.

4. Philpott: Vegetative Endarteritis of Pulmonary Artery Complicating Persistent Ductus, Ann. Int. Med. **2**:948, 1929.

involving the ductus and the anterior wall of the pulmonary artery directly opposite the orifice of the ductus. In the instances reported by Hamilton and Abbott [5] the pulmonary artery is more extensively involved. *Streptococcus viridans* infection was noted in two instances [6] and pneumococcic infection in one.[5]

REPORT OF CASE

History.—A. G., a boy, aged 13, was admitted to the Montefiore Hospital, complaining of cough and fever of ten days' duration. His mother had died at the age of 40 of tuberculosis associated with congenital heart disease. The patient was not cyanotic at birth. At the age of 2 a precordial heave was noted, and on physical examination at that time a diagnosis of congenital heart disease was made. He was under observation at a clinic for cardiac disease, though he had no symptoms except slight dyspnea on climbing stairs. He led the normal active life of a child. At the age of 3 he had whooping cough; at 9, measles, and at 6 "growing pains," but never any other rheumatic manifestations. Ten days prior to admission a dry cough developed, with a fever rising to 103 F. and pain in the back between the shoulder blades. He was weak and rapidly lost weight. On physical examination he was well developed though poorly nourished. His lips and finger-tips were slightly cyanotic. He had a hacking dry cough. His skin was pale brown. There was impaired resonance over both apexes and over the base of the left lung. There was a diffuse precordial heave; the heart was enlarged (cardiac dulness measuring 6 cm. in the second interspace, 8.5 cm. in the third, 12.5 cm. in the fourth and 13.5 cm. in the fifth interspace) and the point of maximal impulse was in the fifth intercostal space 8 cm. to the left of the midline. A systolic and long diastolic thrill were felt over the apex and pulmonic area. There was a rough to and fro murmur over the pulmonic and aortic areas transmitted upward, and a systolic and diastolic murmur at the apex. The liver and spleen were not palpable. Petechiae were absent. The blood pressure was 120 systolic and 30 diastolic. The urine was normal. There was a moderate secondary anemia.

Course.—The boy had a septic fever with excursions from 101 to 105 F. He continued to complain of weakness, and there was a persistent unproductive cough. Six days after admission a dull pain developed in the left upper quadrant, which increased in severity and radiated to the back. Marked tenderness and local spasticity were present. A diagnosis of splenic infarct was made. The blood count showed an increasing secondary anemia; petechial hemorrhages appeared on the hard palate two months after admission, and red blood cells were found in the urine. The dyspnea and weakness became more severe ,and the patient died two and one-half months after admission. *Streptococcus viridans* was twice isolated from the blood stream during life. The clinical diagnosis was congenital heart disease with subacute bacterial endocarditis. The anatomic diagnosis was patent ductus arteriosus, pulmonary stenosis, marked hypertrophy of the infundibulum of the right ventricle, subacute bacterial endarteritis (*Streptococcus viridans*) of the pulmonary artery and the ductus arteriosus, acute embolic hemorrhagic nephritis, multiple infarcts of the lung, anemia infarcts of

5. Hamilton and Abbott: Patent Ductus Arteriosus with Acute Infective Pulmonary Endarteritis, Tr. A. Am. Phys. **29**:294, 1914.

6. Schlaepfer (footnote 2). Philpott (footnote 4).

the spleen, splenomegaly and chronic passive congestion of the liver and lungs. (Only positive observations are described.)

Autopsy.—The body was emaciated (160 cm. in length). Small hemorrhages were visible on the hard palate. Petechiae were present on the skin of the chest, back and abdomen. There was a small amount of straw-colored fluid in the pericardial sac.

Fig. 1.—Pulmonic artery and right ventricle, showing vegetative endarteritis, pulmonic stenosis and hypertrophy of the right ventricle. The arrow points to pulmonic orifice of patent ductus. Reduced from a magnification of × ⅔.

The heart weighed 400 Gm.; it was markedly enlarged. The aortic ring measured 5.5 cm., the mitral 10 cm., the pulmonic 4 cm. at the free edge of the cusps and the tricuspid 10.5 cm. The left ventricular wall was 16 mm. in thickness; the right, from 9 to 11 mm. The heart was globular in shape. There

were several pinpoint hemorrhages over the anterior surface. The epicardial fat was scanty. The infundibular portion of the right ventricle was prominent and bulged forward. The first portion of the pulmonary artery had a fusiform aneurysmal dilatation and a purplish color which contrasted with the white of the aorta. When the heart was opened, both auricles were slightly dilated. The right ventricle showed an increase in size of the infundibular portion. The pul-

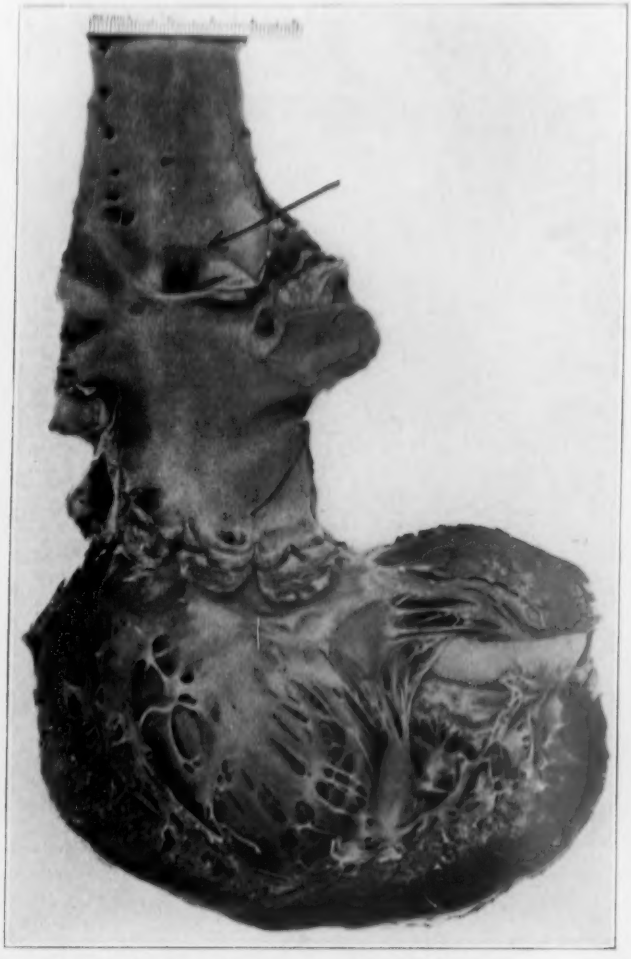

Fig. 2.—Aorta and left ventricle, showing aortic orifice of patent ductus arteriosus. Reduced from a magnification of × ⅔.

monary orifice was definitely narrowed. The cusps were fused and somewhat thickened. There was a communication between the aorta and the pulmonary artery just distal to the arch of the aorta beyond the origin of the subclavian artery. Its lumen was about 1 cm. in diameter, and it entered the pulmonary artery at a point 4 cm. above the pulmonary valve, the highest portion of the aneurysmal bulge. In situ, the arching of the aorta provided an intimal fold

which served as a partial valve over this patent ductus arteriosus. The pulmonary artery showed a striking lesion. It was almost completely occluded by mushy, grayish, friable vegetative thrombi, firmly attached to the wall of the vessel. They extended down to a point just above the free edge of the cusps and up for a short distance into the two main branches of the pulmonary artery. Similar vegetations involved the pulmonary opening of the lumen of the ductus, though none appeared on the aortic side. The mitral, aortic and tricuspid valves were normal. The myocardium was fairly firm but pale. The coronary arteries were normal (figs 1 and 2).

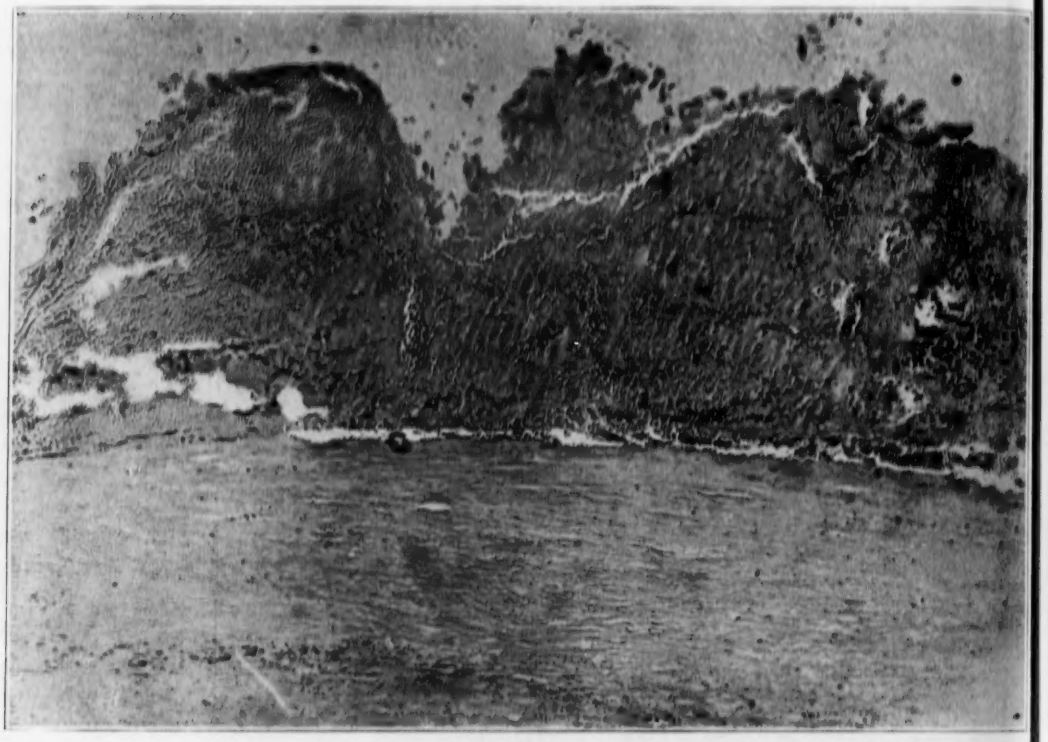

Fig. 3.—Section of pulmonary artery at the site of the vegetative endarteritis. Reduced from a magnification of × 30.

The kidneys were normal in size. The capsule stripped readily; the surface was pale and smooth and was studded with numerous pinpoint hemorrhages. On section, the architecture was distinct; the cortex was studded with minute hemorrhages.

Microscopic Examination.—Areas of hemorrhage were found in the epicardium. In the musculature close to the epicardium were focal accumulations of red blood cells. The musculature showed a moderate degree of hypertrophy. There were no accumulations of lymphocytes or polymorphonuclears in the interstitial tissue.

Section was made through the pulmonary artery at the site of the endarteritis. The normal architecture of the artery was recognizable. The intima was replaced

by a large mass of fibrin and necrotic tissue, masses of bacteria and numerous red blood cells. The underlying media was invaded by polymorphonuclears. The inflammatory reaction extended to the outer coat of the vessel. In the adventitia accumulations of polymorphonuclears were clustered about some of the vasa vasorum. The vasa showed evidence of intimal necrosis, and some lumina were occluded by thrombi (figs. 3 and 4).

Section of the lung showed edema and marked passive congestion. In a large area the alveoli were filled with red blood cells, and there was beginning necrosis of the alveolar walls. The arterioles showed marked thickening of their media.

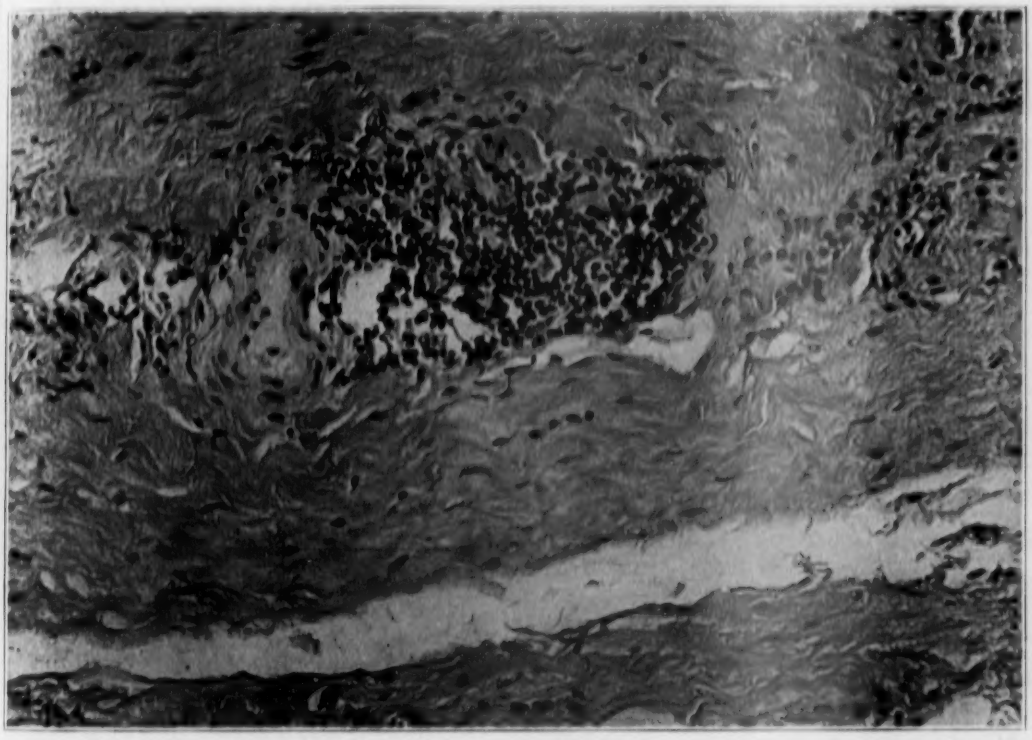

Fig. 4.—Section of adventitia of pulmonary artery, showing perivascular infiltration with polymorphonuclears. Reduced from a magnification of × 240.

Several small arteries and arterioles showed an inflammatory process. The intima was necrotic and was invaded with round cells and polymorphonuclears. The media was somewhat thickened, and the lumen was filled with desquamated intimal cells. The surrounding tissue in the adventitia contained a few round cells. Gram-positive cocci were found in the lumen of several arterioles (fig. 5).

Section of the spleen showed marked congestion. In some of the malpighian bodies there were focal areas of necrosis. Throughout the pulp there were large numbers of polymorphonuclears.

The glomeruli of the kidney were large; the cellular elements were markedly increased. The spaces of Bowman were filled with serum and in places with red blood cells. Some glomeruli showed small hyalinized thrombi in the capillaries,

and in some instances an entire glomerulus was reduced to a small necrotic mass around which was a small number of red blood cells and polymorphonuclears. In one or two instances the space of Bowman contained a crescent-like thrombotic mass, completely epitheliated and showing evidence of organization. Large numbers of tubules in the cortex and medulla were filled with red blood cells. There were focal areas of round cell infiltration in the interstitial tissue which was definitely increased throughout the kidney. There were one or two small infarcted areas in which the tubular elements showed evidence of necrosis.

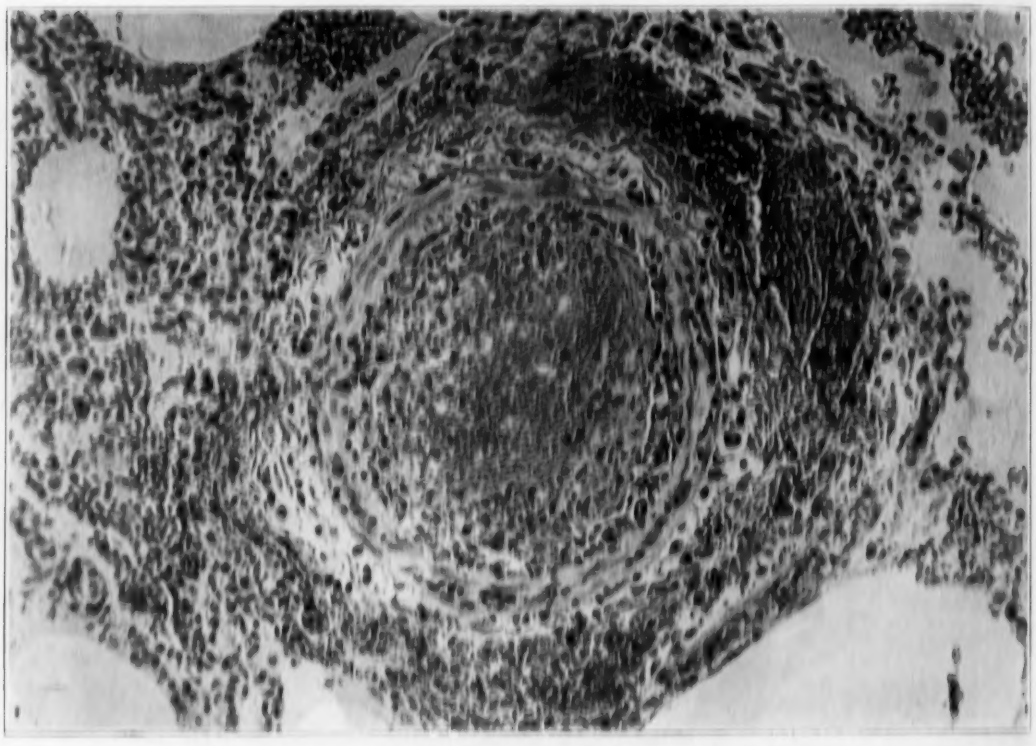

Fig. 5.—Photomicrograph of lung, showing acute arteritis of pulmonary arteriole. Reduced from a magnification of × 240.

COMMENT

A boy, aged 13, with a congenital cardiac defect but in apparent good health developed a *Streptococcus viridans* infection, to which he succumbed within two and one-half months after the onset. The clinical course was characterized by septic fever, progressive weakness, secondary anemia and embolic phenomena in the lungs, spleen and kidney. Autopsy revealed: (1) a patent ductus arteriosus and a congenital pulmonic stenosis with marked hypertrophy of the right ventricle; (2) a subacute bacterial endarteritis (*Streptococcus viridans*) of the pul-

monary artery and ductus arteriosus with large thrombotic masses almost occluding the lumen; (3) no involvement of valves; (4) embolic lesions in the lungs, kidneys and spleen, and (5) acute arteritis of the large and small pulmonary vessels.

Maude Abbott,[7] in an analysis of six hundred and fifty-six clinically significant congenital anomalies, found acute endocarditis in 19.6 per cent. The cardiac anomalies of the "noncyanotic" group, especially bicuspid semilunar valves, defects of the upper part of the interventricular septum and patent ductus arterosus are most frequently the site of infective processes. Persons with defects of the "cyanotic" group who reach adult life, e. g., those who have pulmonic stenosis, are also predisposed to bacterial endocarditis. Patients with complex and serious defects die early, before bacterial infection supervenes.

Relative Frequency of Bacterial Infection in the Different Lesions of the Noncyanotic Group

	Cases	Number	Per cent
Defects at upper part of interventricular septum	54	22	41
Fused semilunar cusps	31	11	35.5
Patent ductus arteriosus	84	23	27.3
Defects at lower part of interventricular septum	15	3	20
Coarctation of aorta	60	12	20
Aortic septal defects	21	4	18

In sharp contrast to the observations given in the accompanying table is the fact that infective endocarditis did not occur in the vicinity of the defect in any of the thirty-two instances of uncomplicated patent foramen ovale nor in nine other cases with defects at the upper part of the interauricular septum; nor did it involve the margins of a defect in the lower part of the interventricular septum, i. e., when this lay at a distance from the auricular ventricular ring. According to Abbott, the frequency of bacterial infection depends on the juxtaposition of the defect to the valvular endocardium.

Of the two hundred and sixty-one cases of the cyanotic group analyzed, ninety-six were cases of pulmonary stenosis (usually associated with septal defect), and among those, acute endocarditis occurred in twenty-six, or 47 per cent. Among the remaining one hundred and sixty-seven cases an infective process was present in only ten instances, or 6 per cent. As Robinson[8] pointed out, the latter small incidence is due to the early death of patients with the more complex defects.

7. Abbott (footnote 1, second reference).

8. Robinson: Relation Between Congenital Malformations of Heart and Acute Endocarditis with Report of Two Cases, Bull. Ayer Clin. Lab. Penn. Hosp. **2**:45, 1905.

REVIEW OF THE LITERATURE

We have collected from the literature a group of relatively simple congenital cardiac defects associated with bacterial inflammation which illustrate clearly the importance of intimal fibrosis in predisposing to bacterial implantation. This fibrosis may be part of the congenital defect or may be due to impingement of anomalous currents on the endocardium.

Patent Ductus Arteriosus.—Schlaepfer [9] reviewed nineteen instances of endarteritis of the pulmonary artery associated with patent ductus. We add three more instances of these associated lesions found in the literature [9] and the instance reported in this communication. In all but five of these a valvular lesion was associated.

The development of infective endarteritis in the instances of patent ductus arteriosus is probably due to mechanical injury by the arteriovenous current of the wall of the artery at, and opposite, the point of entrance of the duct into the pulmonary artery. Boldero and Bedford [10] pointed out that since the pulmonic valve is spared in a large percentage of cases of patent ductus associated with pulmonary endarteritis, the process probably begins in the wall of the artery and spreads to the valves. Posselt [11] noted the frequency of sclerosis of the pulmonary opening of the ductus and of the anterior wall of the artery opposite the ductus opening, and as the following instances indicate, these sites are most frequently invaded by bacteria.

In ten of Schlaepfer's nineteen instances in which the ductus was involved, the vegetations were also on the anterior wall of the pulmonary artery, i. e., opposite the ductus. In Philpott's and in Horder's instances the lesion was also on the wall of the artery opposite the ductus. In eight of the remaining eleven instances the vegetations involved other parts of the wall as well; in only one instance, that of Kidd,[12] were there vegetations on the posterior wall and not on the other walls.

An instructive instance is that of Rickards,[13] in which there was a patent ductus with soft polypoid vegetations on the cusps of the pulmonary valve, the anterior wall of the pulmonary artery, the wall of the ductus, and on the inner lining of the posterior and left extremity

9. Philpott (footnote 4). Posselt: Die Erkrankungen der Lungenschlagader, Ergebn. d. allg. Path. u. path. Anat. **13**:352, 1909. Horder: Infective Endocarditis, Quart. J. Med. **2**:289, 1908-1909.

10. Boldero and Bedford: Infective Endocarditis in Congenital Heart Disease, Involving the Pulmonary Artery, Lancet **2**:747, 1924.

11. Posselt (footnote 9, second reference).

12. Kidd: Embolic Aneurysm on Pulmonary Artery with Patent Ductus, Tr. Path. Soc. London **44**:47, 1893.

13. Rickards: A Case of Ulcerative Endocarditis, Brit. M. J. **1**:640, 1889.

of the transverse part of the arch of the aorta just opposite the ductus. Hochhaus [14] reported a similar aortic localization. The lesion in the wall of the aorta was probably due to a reverse flow through the ductus from the pulmonary artery to the aorta, i. e., a temporary venous arterial shunt instead of an arteriovenous shunt. This is a known clinical occurrence in the transient cyanoses of the "noncyanotic group."

Ventricular Septal Defects.—In the cases of Callender,[15] Hebb [16] and Horder,[17] the localization of a patch of vegetations on the wall of the right ventricle opposite the septal defect illustrates the importance of mechanical stress in determining the locus of infection. The development of vegetations at the site of fibrosis in the septal defect as in cases of Robinson [18] is also suggestive.

Pulmonic and Infundibular Stenosis.—Pulmonic and infundibular stenoses frequently become sites of infective endocarditis. Robinson,[18] Tuley and Moore,[18] Lubarsch [19] and others reported such instances. Lafitte [20] reported an instance of infundibular stenosis with mural endocarditis at the site of the obstruction.

Coarctation of the Aorta.—In coarctation of the aorta a bacterial endarteritis supervenes rarely. Reinfenstein [21] reported a case of pneumococcus endarteritis at the point of coarctation. Libman [22] described a subacute bacterial endarteritis occupying the wall of the aorta just below the constriction. In the instance reported by Mackenzie [23] *Staphylococcous albus* endarteritis was present, and in that of Poynton and Sheldon [24] an ulcerative endarteritis due to a hemolytic streptococ-

14. Hochhaus: Beiträge zur Pathologie des Herzens, Deutsches Arch. f. klin. Med. **51**:1, 1893.

15. Callender: Perforation of Septum Ventriculorum; Clots in Some of the Pulmonary Arteries, Tr. Path. Soc. London **9**:91, 1858.

16. Hebb: Heart with Congenital Defects and Inflammatory Disease, Tr. Path. Soc. London **48**:41, 1897.

17. Horder (footnote 9, third reference).

18. Tuley, H. E., and Moore, J. W.: Report of a Case of Congenital Pulmonary Stenosis with Acute Vegetative Inflammation of Pulmonic Valve and Artery, Am. J. Dis. Child. **13**:426 (May) 1917.

19. Lubarsch: Einiges zur pathologischen Anatomie und Histologie der Endocarditis lenta, Virchows Arch. f. path. Anat. **246**:332, 1923.

20. Lafitte: Retrecissement infondibulaire de l'artere pulmonaire; endocardite vegetante au niveau du retrecissement, Bull. Soc. anat. de Paris **67**:13, 1892.

21. Reifenstein: Two Cases of Mycotic Aneurysm, Am. J. M. Sc. **168**:381, 1924.

22. Libman, quoted by Abbott (footnote 1, first reference, p. 194).

23. Mackenzie: Coarctation of Aorta with Staphylococcus Albus Aortitis, Am. J. M. Sc. **174**:87, 1927.

24. Poynton and Sheldon: Coarctation of Aorta with Ulcerative Aortitis, Arch. Dis. Childhood **3**:191, 1928.

cus. Other instances are reported by Focken [25] and Smith and Hansmann.[26] In all, the infection occurred at a level just below the coarctation.

Bicuspid Semilunars.—Paget,[27] Peacock,[28] Garrod [29] and Osler [30] all emphasized the frequent association of bicuspid valves with endocardial inflammation. Peacock [31] found that in 26 cases of aortic valvular disease, 9, or 33 per cent, probably originated in malformation of the valves. Lewis and Grant [32] reviewed a series of 116 instances of congenital bicuspid valves. Of these, 69 were in adults, and 23 per cent showed a vegetative endocarditis. Of 32 cases in patients less than 20 years of age, 3, or 9 per cent, showed vegetations. Of a series of 31 consecutive instances of subacute infective endocarditis, 8, or 26 per cent, had congenital bicuspid semilunars. The discrepancy between the incidence in these series and in those of other authors may be due to overlooking minor defects.

Lewis and Grant suggested that the predisposition of congenitally fused cusps to bacterial disease may be due to intimal fibrosis or possibly to increased vascularity but present no evidence in support of the latter suggestion. In none of the four instances of fused cusps studied in detail is any mention made of vascularity of the cusps themselves; in case 3 [33] the ridge of one cusp at its attachment to the ring is described as being highly vascular.

Gross [34] supported the view of Köster that bacteria may gain access to the valve through the coronary capillaries, and suggested that the predisposition of congenitally malformed valves to bacterial endocarditis may be due to an arrest of normal vascular regression. Grant,

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25. Focken: Isthmusstenose der Aorta und septische Endokarditis, Ztschr. f. klin. Med. **100**:179, 1924.

26. Smith, F. M., and Hansmann, G. H.: Mycotic Aneurysm of Aorta, Arch. Int. Med. **38**:367 (Sept.) 1926.

27. Paget: On Obstructions in Branches of Pulmonary Artery, Med. Chir. Trans. **27**:29, 1844.

28. Peacock: Malformations of Human Heart, London, 1866, p. 187.

29. Garrod: Malformations of Aortic Valves with Ulcerative Endocarditis, Tr. Path. Soc. London **48**:42, 1897.

30. Osler: On Malignant Endocarditis, Gulstonian Lectures, Lancet, 1885, pp. 415, 459, 505; On the Condition of Fusion of Two Segments of Semilunar Valve, Montreal Gen. Hosp. Rep. **1**:242, 1880.

31. Peacock: On Some of the Causes and Effects of Valvular Diseases of the Heart, Croonian Lectures of the Royal College of Physicians for 1865, London, Churchill and Sons, 1865.

32. Lewis and Grant: Importance of Congenital Defects of Aortic Valves in Causation of Subacute Bacterial Endocarditis, Heart **10**:21, 1923.

33. Lewis and Grant (footnote 32, p. 42).

34. Gross: The Blood Supply to the Heart, New York, Paul B. Hoeber, 1921.

Wood and Jones,[35] in a detailed discussion of the relation of irregularities of the valve to subacute bacterial endocarditis, admit the possibility of embolic infection of valves but consider the superficial irregularity of greater importance. While they show that neither recesses in the form of pockets and crevices nor projections in the form of connective tissue thickenings covered with endothelium can be regarded as offering bacteria a foothold in the valve, they suggest that local degenerative change in the thickened valve with susequent formation of nonbacterial thrombus may offer a foothold for bacterial inflammation.

It is obvious that the exact nature of the relationship between congenital cardiovascular defect and bacterial inflammation is not yet known. The group of cases analyzed suggests strongly the importance of mechanical stress.

SUMMARY

1. An instance is reported of subacute bacterial endarteritis (*Streptococcus viridans*) of the pulmonary artery associated with a patent ductus arteriosus and a congenital pulmonary stenosis. None of the valves were involved.

2. The relationship of congenital defect to bacterial inflammation is discussed.

35. Grant, Wood and Jones: Healed Valve Irregularities in Relation to Subacute Bacterial Endocarditis, Heart **14**:247, 1928.

EMPYEMA OF THE NEW-BORN *

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Empyema of the new-born is a subject which, perhaps justly, because of its apparent rarity, has received scant attention in textbooks on diseases of children. It was not specifically discussed in Abt's "Pediatrics" [1] or in Holt and Howland's [2] textbook. Grulee and Bonar [3] in "Clinical Pediatrics" briefly discussed the subject, as did von Reuss [4] and Finkelstein [5] in their books on diseases of the new-born and diseases of infants, respectively. The reason for this is not far to seek. The rapidity of the progress of the disease to a fatal termination, together with the difficulty of diagnosing fluid in the chest of a new-born infant, has caused the diagnosis of empyema in most of these cases to be made only at necropsy.

It may be stated that by a new-born infant is meant one of 3 weeks of age or less, according to the admittedly somewhat arbitrary classification of von Reuss.[6] Primary pleuritis of the new-born, i. e., pleuritis without accompanying or preceding disease of the lung, has never been described, as far as we can discover. As an accidental observation at necropsy, empyema of the new-born, while not common, is not particularly rare. For example, in a series of seven necropsies on infants under 3 weeks of age who died of pneumonia at this hospital during the past two years, unsuspected empyema was found three times or in 43 per cent of the cases.

* Submitted for publication, June 13, 1930.

* From the Pediatric and Obstetrical Departments of the Rochester General Hospital.

1. Abt, I. A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1923.

2. Holt, L. E., and Howland, J.: Diseases of Infancy and Childhood, ed. 9, New York, D. Appleton & Company, 1926.

3. Grulee, C. G., and Bonar, B. E.: Clinical Pediatrics, New York, D. Appleton & Company, 1926, vol. 3, p. 93.

4. von Reuss, A. R.: Diseases of the Newborn, New York, William Wood & Company, 1929, p. 310.

5. Finkelstein, H.: Lehrbuch der Säuglingskrankheiten, ed. 3, Berlin, Julius Springer, 1924, p. 638.

6. von Reuss (footnote 4, author's preface, page iv).

Empyema of the new-born was first described in 1837 by Billard,[7] who noted this condition in two infants at necropsy, one 3 days old and the other 16 days. Although the disease has not been known to occur in utero, it is possible that this may happen, as Cruveilhier [8] reported finding false membranes on the pleura of a dead fetus whose mother had suffered from a febrile attack. Cornell [9] described a full term, new-born infant in whom all serous cavities contained more fluid than is usual. Légry and Dubrisay [10] reported a case in an infant who died eleven hours after birth. Necropsy showed seropurulent pleurisy and atelectasis and bronchopneumonia of the lower lobes. A streptococcus was recovered from the fluid in the chest. The mother had a streptococcus vaginitis, and the membranes had ruptured twenty-four hours before delivery. It was believed that the pleurisy was secondary to pneumonia resulting from the inhalation of infected amniotic fluid.

The literature on the subject of empyema in the new-born has been reviewed in three principal papers published in successive decades in different languages. Steele,[11] an American, in 1898, mentioned fourteen cases collected by Hervieux and added twenty-five reports from other sources, including the details of one case observed by himself. Steele noted that empyema of the new-born occurred most frequently secondary to sepsis in either the mother or the child. Of interest with regard to this is the evidence of Baron,[12] who found empyema more frequent during the first five days of life than during the remainder of the first month. Steele noted that the incidence of the disease had declined since the prophylaxis of puerperal sepsis had become better understood. He observed that the disease was invariably fatal, and that up to that time no cases had been reported as having been diagnosed during life.

The next important review of the subject was by Gayet,[13] a Frenchman, in 1908. He reviewed sixteen cases, most of which were taken from

7. Billard, C. M.: Traité des maladies des enfants nouveau-nés et à la mamelle, ed. 3, Paris, J. B. Baillière et fils, 1837, p. 579.

8. Cruveilhier: Dictionaire de médecine et chirurgie pratique: Pleurésie, p. 285, quoted by E. A. Graham, in Abt, I. A.: Pediatrics, 1924, vol. 4, p. 79.

9. Cornell, E. L.: The Pneumococcus Found in a Case of Stillbirth, J. A. M. A. **68**:843 (March 17) 1917.

10. Légry and Dubrisay, L.: Infection à streptocique du foetus par contamination buccale, Presse méd. **1**:135, 1893.

11. Steele, J. D.: Pleuritis in the New-Born Infant, with the Report of a Case, Philadelphia M. J. **2**:557, 1898.

12. Baron: Ueber die Pleuritis der Kinder, J. f. Kinderkr. **1**:20, 1843.

13. Gayet, M.: Contribution à l'étude de la pleurésie purulente chez le nouveau-né, Thèse de Paris, 1908. For a brief review of this paper see Comby, J.: La pleurésie purulent chez les nouveau-nés, Arch. de méd. d. enf. **12**:934, 1909.

the literature; like Steele, he concluded that puerperal sepsis was the most frequent cause of pleurisy in the new-born. The germ most frequently encountered was the streptococcus, and he considered that the routes by which infection entered the body were placental, respiratory, umbilical, cutaneous and gastro-intestinal. As a corollary to this, Gayet recommended as prophylactic measures the avoidance of maternal disease, the prevention of premature rupture of the membranes, prevention of infections of the vaginal tract, care of the umbilicus and the avoidance of gastro-intestinal upsets in the infant. Gayet mentioned that roentgenograms might assist in the diagnosis in case of doubt, if the patient was in a hospital where roentgen facilities were available. He stated that the quantity of fluid in the chest may vary from 5 to 80 or 100 cc., that the sooner the disease appears after birth the worse is the prognosis, and that if the patient is untreated, the condition is always fatal.

In 1920, the literature on empyema in the new-born was again reviewed by Rummel,[14] a German. He discussed particularly the three possible periods of infection: (1) intra-uterine, through the placental circulation or through infected amniotic fluid, (2) during labor and (3) after birth. Cases were mentioned illustrating each type. As in the study of Gayet, the streptococcus was given as the organism most frequently encountered.

Past experience indicates that the diagnosis of empyema in the living new-born infant will not be made unless the possibility of this condition is kept in mind by the examining physician. The cardinal signs of the disease, as emphasized by Gayet, are: (1) cough, (2) fever and (3) dyspnea. These are variable, however, for the reason that the reactions of the new-born to disease are not as characteristic as those of older children. Cough, if it occurs, is short, dry and paroxysmal, and is heard characteristically on change of position. Fever, when present, is usually high and remittent. The nervous system of the new-born, as well as the temperature-regulating mechanism, is undeveloped and relatively unstable as compared with later life, which may explain why these symptoms occur in some infants and not in others. Dyspnea is, perhaps, the most constant symptom and may, as in our case, be the first to attract attention. The constancy of dyspnea is probably due to the fact that even at birth the respiratory center is fairly well developed, since the initiation of postnatal life depends on its ability to respond to irritation, and this center is regulated not so much by means of nerve impulses

14. Rummel, H.: Septische Lungen-Pleuraekrankung beim Neugeborenen, Monatschr. f. Geburtsh. u. Gynäk. **53**:336, 1920.

as through the medium of the chemical state of the blood or the hydrogen ion concentration of the cells of the respiratory center itself.[15] The mechanical factors in empyema, such as displacement of the mediastinum and its contents, are constant, regardless of the kind or virulence of the infecting organism and dependent only on the amout of fluid in the chest.

Pallor, cyanosis or jaundice may be present. Edema of the skin and immobility of the affected side have been observed. Signs elicited by percussion and auscultation may be the same as those of pleurisy with effusion in older persons: dulness or flatness to percussion, increased breath sounds on the opposite side due to compensatory emphysema, decreased breath sounds on the affected side due to compression of the lung and bronchial breathing over the compressed lung above the fluid. In the new-born, as in older patients, any type of lung sound may be transmitted through the fluid. The results of auscultation and percussion of the chest of the new-born are particularly uncertain, because mechanical factors incident to the small size of the chest and its round shape permit the transmission of sound from relatively distant parts. Percussion should be very light, more information being gained from sensing the degree of resistance to the plexímetric finger than by the sound elicited. Flatness in infancy is practically pathognomonic of fluid (if neoplasm is ruled out), as flatness rarely occurs in infants with simple pneumonia, as it does in older children and adults.[16]

The most valuable sign of empyema and the only pathognomonic one is the demonstration of fluid within the pleural cavity by means of thoracentesis. The place to perform the puncture is in the region of maximum flatness or dulness. Grulee and Bonar [8] gave the lowest safe point of puncture as the sixth interspace at the angle of the scapula and the optimum point as the seventh interspace in the posterior axillary line. The needle should be of sufficient size to permit the passage of fairly thick pus. The bevel should be short and the point sharp, and a well fitting obturator should always be used. It is preferable to have the infant in the sitting position because a higher column of fluid is obtained than in any other position, as adhesions are practically never present. Probably an attempt should be made to prevent the so-called "pleural shock." To our knowledge this has not been reported in the new-born, but on pleural puncture in young children and infants

15. Gesell, R.: The Chemical Regulation of Respiration, Physiol. Rev. **5**:551, 1925.

16. Holt, L. E.: Empyema in Children, Arch. Pediat. **9**:349, 1892.

Wilensky [17] observed reflex disturbances in the cardiac or respiratory apparatus and, on rare occasions, generalized convulsions. Procaine hydrochloride is highly recommended by Milano [18] as a local anesthetic for thoracotomy in infancy. The small amounts necessary for local anesthesia are well tolerated in the customary strength (1 or 2 per cent) even by very young infants. Care should be taken not to pierce the lung, and enough punctures should be made to convince the physician that pus is not present, or, if present, that it cannot be reached with his needle. It may be necessary to make ten or twelve punctures. This is because the chest should not be opened for drainage until the fluid can be localized, and if fluid is present and cannot be localized for drainage, the prognosis is hopeless.

The great contribution of the past decade to the diagnosis of lesions of the chest in the new-born is the increasing employment of the roentgenogram. At the time Gayet wrote, the roentgenogram was a novelty just beginning to be put to practical clinical use. At the present time, no condition of the chest should be considered thoroughly studied unless a roentgenogram has been taken. This is particularly true in the new-born because of the difficulty of physical diagnosis, and every infant's chest suspected of harboring a pathologic condition should be subjected to roentgenography. If the film is suggestive of fluid, diagnostic puncture should always be made.

Since empyema of the new-born is not a particularly rare observation at necropsy, it would be superfluous to review the cases previously reported. References to these may be found in the works of Steele, Gayet, and Rummel, which have been briefly outlined. The reports of cases of empyema with symptoms beginning in the new-born period and diagnosed and treated during life are, however, of considerable interest. We have been able to find the records of only three such infants. To the reviews of these cases we shall add the details of our own.

The first case was reported by Devraigne [19] in 1908, and was diagnosed by Bar in the clinic of Tarnier. The patient was a premature female infant, normally delivered, and weighing 2,200 Gm. (4 pounds and 9 ounces) at birth. The mother's puerperium and postpartum course were uneventful. The infant was breast fed. At 19 days of age, the child had a high fever, severe enteritis and bronchopneumonia. Two

17. Wilensky, A. O.: Empyema of the Thorax, Surg. Gynec. Obst. **20**:501, 1915.

18. Milano, M.: Pleuresías purulentas en la infancia, Pediatría espãn. **17**:389 (Nov.) 1928.

19. Devraigne, L.: La pleurésie purulente du nouveau-né, Med. prat. **4**:453, 1908.

days later, the fever had disappeared, but an intense dyspnea was present. Pleurisy with effusion was suspected, and on the twenty-seventh day purulent fluid was withdrawn by puncture at the base of the right lung. Staphylococci and a few chains of streptococci were identified in the exudate. On the following day the infant seemed worse, and an intercostal incision was made in the ninth right interspace; 80 cc. of purulent fluid escaped. Fifteen days later, the infant was discharged with a fistula, which soon healed. Devraigne offered no suggestion as to how the infection was acquired, but its occurrence with enteritis suggests a possible origin.

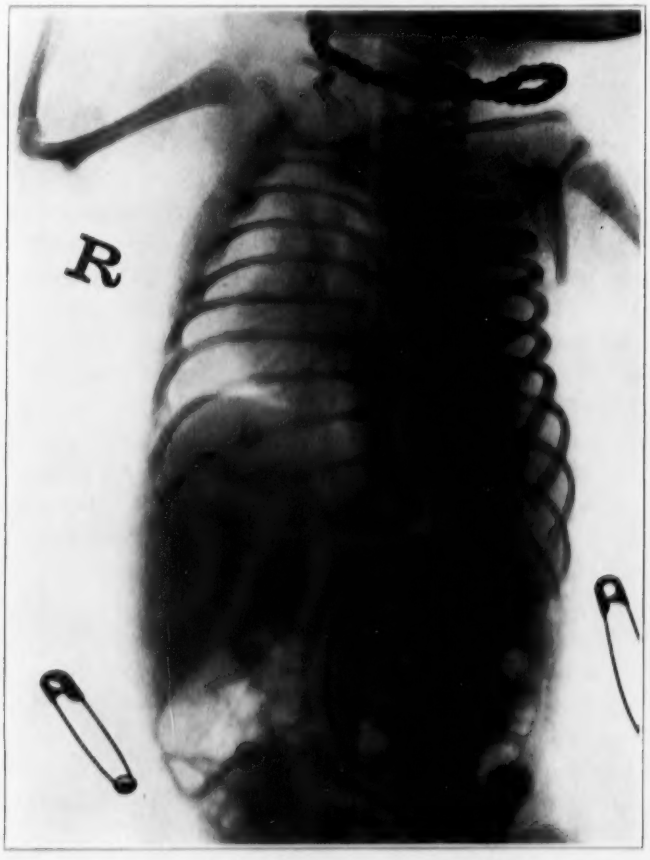
Rummel,[14] in 1920, reported a case of empyema in a full term, normally delivered male infant whose birth weight was 3,400 Gm. (7 pounds and 6 ounces). The symptoms began with attacks of cyanosis and dyspnea on the fourth day. Fever appeared on the following day. The mother of the child had not had a vaginal examination prior to delivery, and her postpartum course was uneventful except for an infected fissure of the left nipple observed on the sixth day. A roentgenogram of the infant's chest at this time suggested atelectasis, pneumonia or pleuritis on the left side. The heart was pushed over somewhat toward the right. The infant was treated by repeated punctures of the chest, a total of 24 cc. of purulent fluid being withdrawn. Death occurred on the ninth day. A hemolytic streptococcus was obtained from the pleural exudate and from a blood culture taken during life. Necropsy showed an empyema of the left pleural cavity secondary to a rupture of a lung abscess the size of a cherry at the base of the left lower lobe. The left lung was compressed and atelectatic. There was, in addition, a serofibrinous pericarditis. Rummel believed that the empyema followed an aspiration pneumonia from regurgitated gastric contents, probably infected through the breast milk.

Spence,[20] also in 1920, reported a series of 204 cases of clinical empyema in infants 3 years of age or less. This included only 3 infants under 3 months of age, and 2 of these died. The youngest of the patients was a male child admitted to the hospital at the age of 14 days with a history of diarrhea of two days' duration. There were definite signs of pulmonary consolidation at the base of the right lung. The weight at this time was 3,140 Gm. (7 pounds). Eight days later, fluid was suspected, and pus was withdrawn by exploratory puncture. A pure culture of *Staphylococcus aureus* was obtained from the pleural exudate. Two blood cultures were negative. The infant was treated by continuous siphon drainage, and recovered.

20. Spence, R. C.: Empyema in Infants and Young Children, Am. J. Dis. Child. **20**:545 (Dec.) 1920.

REPORT OF CASE

In our case, a white male infant, weighing 4,180 Gm. (9 pounds, 3 ounces) at birth, had been delivered after an uneventful labor of six hours. The patient was the second child, and the antepartum and postpartum periods were entirely uneventful. At the age of 4 days, the infant's temperature mounted to 103 F. The breast milk was scanty, and he was given a complementary feeding, which he took eagerly. The temperature immediately dropped to normal. Because of



Empyema of the left pleural cavity, in an infant, aged 11 days.

this, and since nothing abnormal could be found on physical examination to explain the temperature, it was attributed to inanition fever. The weight at this time was 3,720 Gm. (8 pounds and 3 ounces), and it remained at this level with only minor fluctuations until death. A few pustules were present in the skin of the left axilla and the thigh. The temperature continued normal, and on the tenth day circumcision was performed. That afternoon attention was attracted to the child because of grunting respirations. Early the following morning the temperature was 101.6 F., and it rose gradually to 102 F. that evening. There

was marked dilatation of the alae nasi with every inspiration. The infant was slightly pale and jaundiced, but not cyanotic. The anterior fontanel was normally open, flat and not under tension. There was no stiffness of the neck. The pharynx was slightly injected, the tongue moist and moderately coated, and the ear drums appeared normal. The right lung was resonant throughout, with increased transmission of breath sounds. There was dulness throughout the left lung, except at the apex. At the base of the lung, both anteriorly and posteriorly, the breath sounds were diminished and had a bronchial quality. A few fine moist râles were heard anteriorly. The cardiac dulness extended to the right of the sternal margin. The heart sounds were normal and best heard to the right of the sternum. The abdomen was slightly distended but soft. The edge of the liver was palpable 3 cm. below the right costal margin. The spleen could not be felt. The umbilicus was well healed. The circumcision wound appeared exceptionally clean. The knee jerks were bilaterally exaggerated.

A roentgenogram (see accompanying illustration) showed the structures in the left side of the chest obscured by a dense, homogeneous shadow extending from the apex to the base and obliterating the outline of the left side of the diaphragm. The heart and mediastinum were pushed considerably toward the right. The roentgen diagnosis was fluid in the left pleural cavity. With the child in the sitting position, the point of maximum dulness was just below and lateral to the angle of the left scapula. Under local anesthesia with procaine hydrochloride, the pleural cavity was entered with a no. 22 gage Luer needle. Nothing could be withdrawn through this, so another puncture was made with a no. 18 needle, and 30 cc. of a brownish-yellow fluid was aspirated. From this a pure culture of hemolytic *Staphylococcus aureus* was obtained. Following the tap the child's condition seemed much improved, the dyspnea disappeared, and he took his feedings well.

Early the next morning, on the twelfth day of life, the child refused his feeding, and about an hour later he became cyanotic. The respirations were rapid and labored, and he seemed to be in a state of shock. The chest was tapped, and 55 cc. of fluid was withdrawn. Following this the child looked better, but the respirations remained rapid, 80 per minute, and of the Biot type. His temperature was 97.6 F.

An examination of the blood was made, with the following result: hemoglobin (Sahli), 86 per cent; red blood cells, 4,410,000; white blood cells, 5,800; neutrophils, 45 per cent; small lymphocytes, 50 per cent; large mononuclears, 3 per cent, and basophils, 2 per cent. These observations are within the range of normal, except that for hemoglobin, which is about 10 per cent below the average low normal, and that for the white cell count, which is about half the usual average for this age.[21] The urine was acid, amber and slightly turbid, with albumin present (+) and no reducing bodies. Microscopic examination showed an occasional red or white blood cell.

In the course of the morning the child gradually became cyanotic again, and was placed in a Warren-Collins oxygen tent with artificial heat applied to his body. As long as he remained in this tent his color was good, but on his removal cyanosis appeared. Since the baby refused his bottle, as a supportive measure he was given 10 per cent dextrose subcutaneously and intramuscularly[22] and an

21. Lucas, W. P., and Washburn, A. H.: Diseases of the Blood and Blood-Building Organs, Clinical Pediatrics, New York, D. Appleton & Company, 1928, vol. 9, p. 38.

22. Glaser, J.: The Intramuscular Injection of Dextrose, J. A. M. A. 91:772 (Sept. 8) 1928.

intraperitoneal injection of 75 cc. of whole, citrated blood from his father. Both the infant and the father belonged to blood group III (Moss), and there was no cross-agglutination. The child seemed somewhat improved afterward, but his temperature rose gradually to 104 F., the heart tones became somewhat distant, and late that night he died. Death was apparently due to respiratory failure, as the heart continued to beat for several minutes after respirations had ceased. A culture obtained from sinus blood immediately after death did not show growth in three days. Lumbar puncture yielded water-clear, faintly yellow fluid, a normal observation at this age.

Autopsy (Dr. I. Gaspar).—The left lung was entirely consolidated, except at the apex, pushed to the right and covered with a fibrinous exudate. There was 40 cc. of purulent fluid in the left pleural cavity. There were several abscesses, about 5 mm. in diameter, in the lingula (the lower, anterior portion of the left upper lobe which forms the lower border of the cardiac incisura). There were several minute abscesses just beneath the pleural surface of the right lung. The heart was pushed to the right, and there was a moderate degree of parietal pericarditis with some fibrinous exudate on the left side. The peritoneal cavity contained free blood with some clots. Apparently, very little of the blood injected had been absorbed. The spleen was only slightly enlarged, dark red and fairly firm. There was no gross evidence of phlebitis of the umbilical vein or the dorsal vein of the penis.

The impression was that an aspiration pneumonia, abscesses of the lung and parapneumonic empyema developed either from infected amniotic fluid or from regurgitated gastric contents. The cutaneous pustules observed at the age of 3 days must also be considered as a possible portal of entry for infection. It is interesting that one of the cardinal signs of empyema in infancy, cough, was absent in our case.

COMMENT

The series of four cases described is, of course, too small to permit the drawing of any conclusions. Nevertheless, some lessons may be learned which may prove of value in the future. Both of the infants who died were treated by repeated punctures of the pleural cavity; the two who survived were treated by continuous drainage through an intercostal incision, one by simple drainage and the other by siphon drainage. Both infants who died had abscesses of the lung; in our case these were multiple. It is doubtful if the prognosis in these cases would have been better had freer drainage been employed, but in a condition as desperate as empyema in the new-born the evidence is much in favor of intercostal drainage. In view of the rapidity with which the disease usually progresses to a fatal termination, it would seem that operation should be performed as soon as the diagnosis is established.

Staphylococci and streptococci were found in one infant who survived, and a pure culture of staphylococcus was obtained from the other

surviving infant. A hemolytic streptococcus was recovered from one infant who died and a hemolytic staphylococcus from the other. It seems curious that pneumococci were not found in any of the cases. Devraigne [18] suggested that the bad prognosis of empyema of the newborn as compared with empyema in older children is due to the fact that in the former cases streptococci and staphylococci are the predominating organisms, while in the latter the organism is most frequently pneumococcus.

The beneficial effect of the oxygen tent in our case suggests that the employment of this therapeutic measure might have been instituted to greater advantage as soon as the infant began to have trouble in breathing, instead of waiting until the cyanosis had become a prominent symptom. That the blood given the infant intraperitoneally was not absorbed may, perhaps, have been due to circulatory weakness. It is highly probable that the transfusion would have been of much more benefit had the blood been given intravenously or into the sinus. Intramuscular injections of dextrose and subcutaneous injections of saline should be given, as in our case, as soon as difficulties in feeding begin.

SUMMARY AND CONCLUSIONS

The subject of empyema in the new-born is briefly reviewed, and the details of four cases (including one of our own) diagnosed during life are given.

In examining the chest of a new-born infant when pulmonary disease is suspected, the possibility of empyema should be kept in mind, and a roentgenogram should always be made. If fluid is suspected, diagnostic thoracentesis should always be performed.

In view of the rapidity with which the disease usually progresses to a fatal termination, supportive measures, such as intravenous or intrasinus transfusion, should be carried out as soon as the diagnosis is made. The parenteral administration of dextrose and saline should be started as soon as difficulty in feeding occurs. Oxygen should be administered by an effective method as soon as dyspnea is observed.

In the four cases of empyema of the new-born diagnosed during life, two infants treated by intercostal incision and drainage recovered and two treated by multiple punctures of the pleural cavity died. It therefore seems that intercostal incision and drainage is the method of choice, and this operation should be performed as soon as the diagnosis is positive.

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ULCERATIVE LARYNGITIS DUE TO CORYNEBACTERIUM ULCERANS *

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Diphtheria, in its local manifestations, is essentially a capillary toxic process inducing necrosis of the affected tissue. This necrosis does not ordinarily lead to deep ulceration; the resulting inflammatory reaction induces the exudation of considerable fibrin, which, with the necrotic tissue and inflammatory cellular elements, forms a covering of varying thickness firmly attached to the affected surface. When this membrane is removed, a defect, the diphtheritic ulcer, is produced; the necrobiotic process is so superficial that the ulcer is usually shallow and involves only the mucosal surface. If the membrane is removed, the ulcer is rapidly covered by a new pseudomembrane composed largely of fibrin and erythrocytes; rarely, usually in mixed infections, is there deep-seated necrosis and ulceration, with subsequent scar formation. In general, the mucosal defect is covered by epithelium regenerated from the adjacent intact areas during the healing process.[1]

In the trachea, owing to the presence of the columnar epithelial lining, the local reaction is modified. Pseudomembranous sheets apparently may cover intact mucosa by the exudation of fibrin, which is displaced by ciliary action. The upper part of the larynx and the true vocal cords, which are lined by stratified squamous epithelium, are rarely affected unless there is pharyngeal involvement. When a pseudomembrane is removed from these areas, the resulting ulcer does not extend beyond the mucosa, for here the mucosal connective tissue is only loosely connected with the underlying tissue. Where there is

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1. MacCallum, W. G.: Text-book of Pathology, ed. 2, Philadelphia, W. B. Saunders Company, 1920, p. 574. Kaufmann, E.: Lehrbuch der speziellen pathologischen Anatomie für Studierende und Aerzte, ed. 7, Berlin, G. Reimer, 1922, vol. 1, pp. 237 and 476. Adami, J. G., and McCrae, J.: A Text-book of Pathology for Students of Medicine, Philadelphia, Lea & Febiger, 1914, p. 529.

deep-seated ulceration, organisms other than the Klebs-Löffler bacillus, a mixed infection or an anomaly of the larynx are usually found.

The following references to similar cases are found in the literature. Hirsch [2] described a group of cases with severe constitutional symptoms and proportionately less pronounced local symptoms, in which the epiglottis showed moderate edema and the larynx and arytenoid cartilages showed edema and deep-seated ulceration. Such cases healed spontaneously within ten days without subsequent fibrosis. No membrane was noted, nor was the Klebs-Löffler bacillus found. Fusiform bacilli were common, but Hirsch recorded no cultural characteristics. Beck's case [3] showed an ulcerative and membranous laryngitis and perichondritis. The arytenoid cartilages were separated and coughed up. From the multiple abscesses developing in the patient's body during the course of the disease, hemolytic streptococci were isolated; Klebs-Löffler bacilli were found in the blood. Locally, a mixture of the two organisms was obtained. In Meserve's case [4] only a superficial ulceration, not extending into the muscular layer of the larynx, was present. This was associated with a papilloma of the cord and marked pseudomembranous formation.

Ribbert [5] expressed the opinion that pronounced ulceration can occur only in the presence of congenital defects or anomalies. In a careful search of the literature we were unable to find a single case of deep laryngeal ulceration (though the aforementioned cases have a bearing on our discussion) either due to Klebs-Löffler bacilli or occurring without the presence of pseudomembrane at the affected site or with but little membrane present when not artificially removed. The following case we believe is the first of the type to be reported.

REPORT OF CASE

History.—S. F., white female infant, aged 9 months, was admitted to the Willard Parker Hospital on Sept. 29, 1928, with an indefinite history of having refused food five days before admission, of having vomited two days before admission and of having begun to cough and show inspiratory difficulty on the day preceding admission. Physical examination revealed an acutely sick infant, pale and markedly croupy. The throat was mildly injected, but no membrane was present. The tonsils were not enlarged. The larynx was edematous and congested. The lungs were normal on percussion, and sounds transmitted from the laynx were heard on auscultation. The heart was hyperactive, but the sounds were not impaired. The abdomen and reflexes were normal. Within two

2. Hirsch, O.: Polypen bei Ozaene, Monatschr. f. Ohrenh. **63**:605, 1929.

3. Beck, K.: On Cartilaginous Necrosis of Larynx in Diphtheric Cases, Acta oto-laryng. **6**:196, 1924.

4. Meserve, E. A.: Diphtheria of the Larynx Associated with Papilloma of the Larynx, Boston M. & S. J. **185**:568, 1921.

5. Ribbert, quoted by Beck (footnote 3).

hours of admission, the pulse became so feeble as to be hardly perceptible. The child died two and one-half hours after admission. The clinical diagnosis was catarrhal laryngitis, laryngeal obstruction and asphyxia.

Autopsy.—Autopsy was performed ten hours post mortem (M. J.). The body was that of a well developed white female infant whose face was mottled a deep red and whose lips were cyanotic. The faucial tonsils were slightly enlarged and firm and had nonulcerated velvety surfaces. On the surface of the right

The specimen reveals an ulcerated and ragged right vocal cord. The left vocal cord is entirely destroyed by the ulcer.

tonsil were three small, soft, blackened areas not covered by exudate and loosely attached to the surrounding tissue. These areas extended for about 1 mm. into the tonsillar tissue.

Along the right border of the epiglottis, apparently extending caudad into the larynx, there was a narrow blackened strand of exudate, firmly attached to the epiglottic surface. This strand was soft and friable and was bordered by a narrow hyperemic zone.

The larynx, looked at from above, was completely closed; it did not even admit the tip of scissors, 2 mm. wide. Within the larynx, both vocal cords were ragged and ulcerated, and their free edges and adjacent cord tissue were friable, but intimately a part of the organ. This tissue was a black-green, shading off into the normal gray in the external (attached) portions. The ulcerated area on the left extended to the perichondrium of the cartilages. The entire left cord was destroyed.

The lungs showed a diffuse congestion. The spleen weighed 34 Gm.; it was firm and rubbery, its capsule tense, its cut surface deeply reddened, its corpuscles prominent. The mesenteric, iliac and periaortic lymph nodes were enlarged and firm. The Peyer's patches were enlarged and hyperemic; discrete petechial-sized hemorrhages were present in the appendical mucosa. The other organs were not grossly altered; the liver lobules were distinctly outlined, the kidneys and heart showed no changes, other than postmortem appearance (dulling of cut surface, bogginess), and the suprarenals were not congested.

Microscopic examination showed marked edema and necrosis of the lymphoid follicles of the appendix, lymph nodes and spleen, marked congestion of the splenic sinuses and a few hemorrhages into the lymphoid tissue of the appendical mucosa. The lungs showed great congestion of the alveolar capillaries, which in places were filled with hyalin-like thrombi. Sections taken from pieces of striated muscle from the neck showed large recent hemorrhagic areas spreading from the vicinity of blood vessels, the walls of which were homogeneously stained, structureless and broken in places. Within these clefts, the effects of recent hemorrhages could be seen. The liver showed a slight central sinusoidal congestion, but the kidneys and suprarenals were unchanged.

Sections through various parts of the laryngeal ulcer showed the surface covered by a granular, amorphous, greenish-yellow débris (resembling hemosiderin) mixed with well preserved erythrocytes and shadows. Here and there were a few squamous epithelial cells, very poorly stained, with pyknotic nuclei and a discrete, homogeneously acidophilic muscle fiber or group of such fibers without visible striations (longitudinal or transverse) or nucleus. Little fibrin was demonstrable in this ulcerated area; numerous masses of gram-positive bacilli and a few cocci were present. A section taken just beyond the ulcerated area showed the stratified squamous epithelium to be necrotic, the cell outlines poorly defined, the cytoplasm of a muddy, acidophilic hue and the nuclei markedly pyknotic, fragmented or entirely absent. The underlying connective tissue showed a pronounced vascular congestion, a few recent hemorrhages and a moderate polynuclear cell infiltration. No fibrin was demonstrable. Similar changes were found in sections of the epiglottis on the affected side. Sections of larynx through the vocal cords and wall and the epiglottis on the unaffected side showed only marked vascular congestion and some small recent hemorrhagic areas in the subepithelial connective tissue. No epithelial changes were demonstrable.

Bacteriologic Investigation.—Smear from the ulcer showed a few diphtheria-like bacilli and a few staphylococci and streptococci. Pure cultures of the bacilli were ultimately obtained; in from four to twelve hours these showed polar bodies in some forms, while others were uniformly stained. Older cultures contained numerous coccoid forms.

The organisms were nonmotile, had no capsules or spores, were gram-positive, and did not retain the acid-fast stain. They grew rather easily on dextrose-serum agar and semisolid agar, forming irregular-edged colonies about 0.5 mm. in diameter. On blood agar, slight hemolysis occurred. A pellicle was formed

on ascitic fluid and dextrose beef infusion broth. Dextrose, maltose and dextrin were fermented; mannite, saccharose and lactose were not fermented. Litmus milk was not altered, nor was indol produced in eight days. Nitrates were not reduced. Gelatin was slowly liquefied in eighteen days. The organism was killed by heating at 56 C. for ten minutes.

Through the courtesy of Dr. Ruth Gilbert of the New York State Department of Health Laboratories, the effects of animal inoculation with the organism were studied. Guinea-pigs inoculated intracutaneously developed marked lesions at the site of inoculation, the reaction being almost as intense in the animal protected with diphtheria antitoxin as in the nonprotected one. Guinea-pigs inoculated subcutaneously with the culture grown in toxin broth developed open ulcers at the point of inoculation, the one on the guinea-pig unprotected with the antitoxin being somewhat larger than the one on the control.

In our own laboratory we repeated the injection of the organisms and injected the filtered broth in which the organism had been grown; necrotizing lesions similar to those produced by the culture itself developed in the guinea-pig. Diphtheria antitoxin injected at the same time did not seem to protect the tissues at the site of injection. Five guinea-pigs were used in each experiment.

Further studies in our laboratory of the viscera of guinea-pigs inoculated subcutaneously with the culture and subsequently killed after periods ranging from one to eight days showed no congestion or hemorrhages except in the mucosa of the small intestines, where numerous petechiae were regularly found in animals killed after the second and before the sixth day. In many such areas the entire gastric and small intestinal mucosa was covered with innumerable hemorrhagic areas. At no point was ulceration or necrosis present. Culture of these areas, as well as blood cultures taken during life, were sterile. The adrenals showed no congestive or hemorrhagic lesions in animals killed between the second and fourth days. The muscle fibers of the heart, and the kidneys and the liver showed no changes.

COMMENT

Anatomically, this case differed from the usual type of diphtheritic involvement of the larynx because of the extreme necrosis and ulceration and the small amount of fibrinous or cellular exudate. The unilateral situation, the extensive hemorrhages into the tissues of the neck and the absence of morphologic changes in the heart, liver, kidneys and suprarenals—organs which frequently show marked congestive, hemorrhagic or degenerative changes—further differentiated this from the usual type of lesion caused by the Klebs-Löffler bacilli.

Bacteriologically, the bacillus isolated differed from *B. diphtheriae* by its failure to reduce nitrates, its ability to liquefy gelatin and to change rapidly to coccoid form in the twenty-four hour culture. This bacillus corresponded to the organism isolated by Gilbert and Stewart,[6] the *Corynebacterium ulcerans.* It, like *C. ulcerans,* experimentally produced necrosis and ulceration of the skin at the site of inoculation with but slight fibrin exudation. Diphtheria antitoxin did not appreciably protect

6. Gilbert, R., and Stewart, F. C.: Corynebacterium Ulcerans; Pathogenic Microorganism Resembling C. Diphtheriae, J. Lab. & Clin. Med. **12**:756, 1927.

an animal against the development of the lesions induced by inoculation with the organism or culture filtrate intracutaneously or subcutaneously. These organisms, which we believe are a species related to the diphtheria bacillus, produce a distinct soluble toxin for which a neutralizing antitoxin can be prepared, which will also protect somewhat against diphtheria toxin (30 units per cubic centimeter). Schick tests made on experimentally infected animals were negative.

This organism was first isolated from the throats of healthy people or people with "slight colds," and the authors suggested its etiologic significance in inflammatory or ulcerative lesions of the nose and throat. No fatal case or one of extensive ulceration due to this organism is on record. We believe that this organism was the etiologic agent in our case, and that it was locally implanted on the larynx of a patient with a slight "cold." It may be that more intensive bacteriologic study of cases of diphtheria, especially of cases in which serum proves ineffectual though administered early in the course of the disease, will reveal this organism. The use of a mixed diphtheria and *C. ulcerans* antitoxin may be worthy of trial.

SUMMARY

1. A case of fatal ulcerative laryngitis due to an atypical diphtheria-like organism and producing only a slight fibrinous reaction is reported.

2. The organism cultured from a laryngeal ulcer is identified as the *Corynebacterium ulcerans* of Gilbert and Stewart, previously isolated only from nonfatal upper respiratory infections. Both organisms produce extensive necrosis and ulceration without the formation of typical diphtheritic pseudomembrane.

3. The immunologic study of cases of diphtheria not responding to antitoxin is suggested.

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JUVENILE EMBOLIC GANGRENE OF AN UPPER EXTREMITY *

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This case is reported because it presents two uncommon and interesting conditions in the same child, namely, aortic stenosis of rheumatic origin and embolic gangrene of the right hand.

REPORT OF CASE

A boy, aged 7 years and 11 months, was admitted to the Post-Graduate Hospital on Nov. 25, 1927, for tonsillectomy and adenoidectomy. The past history was irrelevant, except for frequent sore throats over a period of three years. On physical examination the tonsils were hypertrophied, and the heart presented a blowing systolic murmur that was not transmitted and the maximum intensity of which was at the third interspace at the left border of the sternum. There were no subjective symptoms. Owing to an epidemic of sore throat in the wards, the patient was not operated on.

He was readmitted to the hospital on Jan. 30, 1928, with dyspnea as the chief complaint. On close questioning, a history of indefinite pains ("growing pains") in both legs over a period of three years was brought out. There had been attacks of dyspnea at times since infancy. On the day of admission, when the patient was ascending a flight of stairs, he had a sudden attack of dyspnea that was severe and lasted for one-half hour. There was no history of edema or hemoptysis; however, he had had a chronic nonproductive cough at intervals for the three preceding years. The positive physical observations were as follows: There were hypertrophied tonsils and cervical glands that were slightly enlarged and palpable bilaterally. There was a palpable thrill over the right carotid artery with a rough systolic murmur in the same area on auscultation.

The apex of the heart was 11 cm. to the left of the midsternal line. The heart sounds were transmitted well, and the rhythm was regular. There was a rough systolic murmur over the entire precardia. The point of maximum intensity was in the second interspace just to the right of the sternum in the aortic area. There were no physical evidences of decompensation. The diagnosis was aortitis, aortic stenosis and mitral insufficiency of rheumatic origin.

With rest in bed, the dyspnea and precardial pain disappeared. On the sixteenth day in the hospital, after marked improvement in the clinical condition, a tonsillectomy and adenoidectomy were done. Following the operations, there was no febrile reaction, but the heart's action was irregular, without increase in rate.

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* Submitted for publication, May 7, 1930.

* From the Cardiac Division of the Pediatric Department of the New York Post-Graduate Medical School and Hospital.

From this time until the thirty-ninth day in the hospital, the day of discharge, the pulse remained regular and the rate normal.

Repeated attempts at auscultatory blood pressure readings were made with poor success by virtue of the loud systolic murmur transmitted down into the left arm. The sounds were very weak in the right arm. By palpation, the systolic blood pressure varied at times from 80 to 90.

All laboratory procedures gave negative results.

On the thirty-ninth day in the hospital (March 11), the patient was discharged without symptoms. The physical observations were the same as they were on admission, and the patient was considered improved.

On April 12, 1929, the patient was readmitted to the hospital. The chief complaint was swelling of the right arm and leg, with a bluish discoloration of the right hand. Since the last admission to the hospital, a period of almost a year, the patient had been up and about with no symptoms. One month prior to this admission, he began to suffer from weakness. Three days prior to this admission he had two generalized convulsions, lasting about two minutes each. They occurred twenty minutes apart. Following the last convulsion, the patient lost consciousness, stiffened and became cyanotic. He gradually regained consciousness over a period of half an hour. Within a few hours following recovery, his right arm and leg became swollen. The swelling had persisted until the time of admission, and the right hand had assumed a deep purplish color.

On examination, the patient was extremely pale and appeared acutely ill. The respirations were labored and shallow, and there was impaired resonance with both coarse and fine râles in the bases of both lungs posteriorly.

The area of cardiac dulness was increased, both to the left and to the right. The sounds were muffled. There was a systolic and diastolic murmur over all of the precordia, with the maximum intensity in the second right intercostal space to the right of the sternum. A faint thrill was diffusely scattered over the entire precardia. The liver and spleen were markedly enlarged and tender.

The abdomen presented shifting dulness and slight tenderness, indicating the presence of fluid. The scrotum was slightly edematous.

The right hand presented marked swelling with discoloration (radial distribution), varying from blue to deep purple. No pulse was present, and the member was cold on palpation. The left radial pulse was palpable, but was very weak. Both brachial pulses were palpable.

Both lower extremities were edematous, the right more than the left, and pulsation in the dorsalis pedii was absent. The femoral pulse was palpable, but weak bilaterally.

Scattered irregularly over the calves of both legs, as well as on the right forearm, were small isolated patches of bluish discoloration, apparently due to minute emboli.

The following diagnoses were made: aortitis; aortic stenosis; mitral insufficiency and stenosis of rheumatic origin with chronic passive congestion of the lungs, liver and spleen; ascites; cardiac decompensation; embolism of the right radial artery; minute superficial emboli of the skin of the calves of both legs and the right forearm, and secondary anemia.

On the third day in the hospital the general condition remained about the same, except that the gangrenous area of the hand was turning black and was becoming more demarcated (see accompanying figure).

A surgical opinion by Dr. Edward Peterson advised the following: "Embolic gangrene of right hand and forearm. Cannot get pulsation in forearm or arm. Owing to the serious cardiac condition I advise conservative or palliative measures for the present. Embolectomy to be considered with amputation of the gangrenous parts later."

On the sixth day in the hospital the edema of both the arm and the legs had practically disappeared, and the demarcation of the gangrene of the right hand was complete.

On the tenth day in the hospital general edema began, and from then until death became progressively worse. The pulse became extremely rapid and at times was imperceptible. The patient grew progressively worse, the heart action becoming weaker and the edema greater. He died on the fourteenth day in the hospital.

Right hand of patient, showing gangrenous area.

COMMENT

Aortic stenosis is uncommon in childhood. Polynton [1] encountered it in only 2 of 500 cases of heart disease.

Gangrene of the extremities, while uncommon, is sufficiently interesting to appear in the literature occasionally. Martin and Shore [2] reviewed the literature fully in their treatise on "Juvenile Gangrene."

1. Polynton, quoted by Garrod, Batton and Thursfield: Diseases of Children, New York, Longmans, Green & Company, 1913, p. 447; quoted by Griffith, J. P. C.: The Diseases of Infants and Children, Philadelphia, W. B. Saunders Company, 1919, vol. 2, p. 150.

2. Martin, Walton; and Shore, Benjamin Rice: Juvenile Gangrene, Ann. Surg. **88**:725, 1928.

The most frequent etiologic factor is acute infection, cases having been reported as follows: typhoid fever, typhus fever, scarlet fever, diphtheria, measles, pneumonia, both lobar and bronchopneumonia, appendicitis, tonsillitis, chorea and purpura, as well as various cardiac conditions.

One of the most interesting cases reported was that by Wright.[3] It was a case of bilateral gangrene of the feet following tonsillectomy, in which there was a complicating cardiac lesion.

Barraud [4] collected a large number of cases following acute infection. Hoopman [5] reported a case similar to our case—gangrene of the foot caused by a cardiac lesion in an infant. Khantz [6] reported a number of cases, stressing one in which the gangrene seemed to be without any demonstrable etiologic factor. An occasional case of Raynaud's disease is reported. Every year or so, as in our case, gangrene of the extremities in childhood is reported with a prefatory remark that the rarity of the condition has occasioned the report, and accompanying photographs show the lesions.

The physiology and pathology of the subject are treated exhaustively by Martin and Shore.[2]

CONCLUSIONS

1. A case of aortic stenosis of rheumatic origin with an accompanying embolic gangrene of the right hand in a child is herein reported.
2. This case is reported because of its clinical interest and rarity.

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3. **Wright, I. S.:** Bilateral Gangrene of the Feet Following Tonsillectomy, Am. J. Dis. Child. **37**:121 (Jan.) 1929.

4. **Barraud, S. Weber:** Extremitätengangrän im jugend Alter nach Infections, Krankheiten, Deutsche Ztschr. **74**:237, 1904.

5. **Hoopman, F. W.:** Gangrene of Foot in Infant Caused by Cardiac Lesion, M. J. Australia **1**:288, 1924.

6. **Khantz, A. V.:** Spontane Extremitäten Gangrän im Kindesalter, Ztschr. f. Kinderh., 1914, part 1, vol. 2.

Progress in Pediatrics

I. THE ROENTGENOGRAPHIC AND PATHOLOGIC ASPECTS OF CONGENITAL OSSEOUS SYPHILIS *

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The skeletal lesions of congenital syphilis have been exhaustively studied by European roentgenologists and pathologists, particularly in Germany and France, but in this country and Great Britain limited attention has been paid to this aspect of the disease. One seems justified, therefore, in attempting an exposition of this subject in English based on the study of roentgenograms of the bones of 102 patients with congenital syphilis, in 24 of whom gross and microscopic examination of pathologic material was made.

The histopathology of congenital syphilis of the bone is still obscured by many unsolved problems. Both pathologists and roentgenologists have entered into the controversy regarding many debatable points. In the following study, undertaken with the cooperation of certain members of the intern, pathologic and x-ray staff of the Babies' Hospital, which aims to be essentially practical, the controversial points will be touched on only lightly, since the object is to limit the scope to the fundamental features as correlated by roentgenologic and histopathologic examinations.

HISTORICAL DATA

A presentation of this subject would be incomplete without a chronologic list of those who have made important investigations in the same field, thus demonstrating the increasing length of the base line of endeavor that has lightened the task of successive workers.

Nils Rosen, of Uppsala,[1] in 1778, was the first to emphasize the value of skeletal examination in every case of congenital syphilis. Underwood [2] in 1789 and Mahon [3] in 1804 published a report of clinical

* From the Babies' Hospital and the Department of Diseases of Children, Columbia University.

1. Rosen, N. R.: Traité des maladies de l'enfance, Paris, P. G. Canelier, 1778.

2. Underwood, M.: Treatise on the Diseases of Children, London, J. Mathews, 1789, p. 361.

3. Mahon, P. A.: Histoire de la médicine clinique, Paris, Buisson, 1804, p. 455.

observations. In 1810, Bertin [4] described the successful treatment with mercury of an infant, aged 35 days, with epiphysial swellings. In 1818, Lagneau [5] described periostitis. In 1834, Valleix [6] reported a case of "pustulous exanthemas" in an infant 35 days of age with paralysis of all extremities. In 1847, Trousseau [7] mentioned the swellings of the short bones of the extremities in the disease. In 1853, Bednar,[8] of Vienna, described tenderness and paralysis of the extremities. In 1854, Diday [9] and Combessis [10] made valuable clinical studies. In 1861, Henoch [11] described typical lesions of the humerus in two infants with paralysis of the arms which cleared up under treatment with mercury. He understood the underlying syphilitic disease.

In 1861, Bouchut,[12] Jellinek [13] and Winge,[14] in 1862, Howitz [15] and Mayr,[16] and in 1864, von Zeissl [17] and Lancereaux [18] published a variety of case reports. Bone lesions, however, were considered rare in congenital syphilis even by such authorities as Lancereaux, Trousseau and Diday, as all three mentioned the comparative rarity of pathologic changes in the bones in this disease. Von Bärensprung's [19] book, published in 1864, mentioned three cases of osseous syphilis, but the entrance

4. Bertin, R. J. H.: Traité de maladie vénérienne, ed. 5, Paris, Gabon, 1810.

5. Lagneau, L. V.: Exposé des diverses méthodes de traites la maladie vénérienne, Paris, Gabon, 1818, p. 406.

6. Valleix, F. L. J.: Case Report, Bull. Soc. anat. de Paris **9**:169, 1834.

7. Trousseau, A.: Syphilis des enfants du prémierage, Arch. gén. de méd. **15**: 145, 1847.

8. Bednar, A.: Die Krankheiten der Neugeborenen, Vienna, C. Gerold, 1853, vol. 4, p. 227.

9. Diday, P.: Traité de la syphilis de nouveau-nés, Paris, V. Masson, 1854, p. 134.

10. Combessis, D. M.: Causes qui retardent la consolidation des fractures chez les enfants, Gaz. d. hôp. **27**:163, 1854.

11. Henoch, E.: Beitrag zur Kinderheilkunde, Berlin, A. Hirschwald, 1861, p. 192.

12. Bouchut, E.: Traité des maladies des enfants, Paris, J. B. Baillière et fils, 1861.

13. Jellinek, L.: Beitrag zu Lehre von hereditäre Syphilis, Wien. med.-Halle **2**:259, 1861.

14. Winge, E.: Syphilis and Rachitis, J. f. Kinderkr. **41**:122, 1861.

15. Howitz, O.: Ueber Syphilis Knochenleiden bei Kindern, in Behrend: Syphilologie **3**:601, 1862.

16. Mayr, F.: Syphilis hereditaria, Jahrb. f. Kinderh. **4**:219, 1862.

17. Von Zeissl, H.: Lehrbuch der Syphilis, Stuttgart, Ferdinand Enke, 1864, p. 649.

18. Lancereaux, E.: A Treatise on Syphilis, Tr. by G. Whitley, London, New Sydenham Society, 1868-1869, p. 550.

19. von Bärensprung, F. G. F.: Die hereditäre Syphilis, Berlin, A. Hirschwald, 1864.

of Ranvier [20] into the field of study in the same year marked the first milestone of progress. He reported to the Societé de biologie of Paris the case of an infant in whom autopsy showed in addition to manifest visceral lesions of syphilis the complete separation of all epiphyses from the shafts of the long bones. To this he gave the name "décollement," a term which to date has not been improved. In the same year, Ranvier was the first to mention "arrêt d'ossification" as a paramount manifestation of congenital syphilis. Bargioni [21] reported the detailed pathologic changes of osseous lesions, and Fournier [22] emphasized the value of careful examination of the skeleton for evidence of the disease and reported the treatment of two patients with potassium iodide. About the same time, Fuerth [23] demonstrated a case of epiphysial separation. In 1868, Lewin [24] reported epiphysial separation in living infants. In 1869, Ödmansson [25] reported costochondral separation, and Gueniot [26] recorded an important case. Wegner [27] published his classic treatise in 1870, followed by the clinical and pathologic studies of Parrot [28] in 1871-1873.

As regards the histopathology of osteochondritis, the observations of Parrot and of Wegner are almost identical, except that the former emphasized the participation of the periosteum and perichondrium in the process, and he may be considered as having first established osteochondritis as a distinct clinical entity. His classic description of pseudoparalysis from the clinical and anatomic standpoint has left little to be added by subsequent medical writers. Every student is familiar with Parrot's pseudoparalysis. To Wegner one is in equal debt for the first precise histopathologic description of osteochondritis, which he divided into three stages, since known as Wegner's osteochondritis. Parrot took marked exception to Wegner's conception of an inflammatory origin of the syphilitic process and defined it as "dystrophy syphilitique,"

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20. Ranvier, L. A.: Syphilis congenitale, Gaz. méd. de Paris **39**:596, 1864.

21. Bargioni, D. G.: Ascesso articulo gomme della ossa in neonato, Sperimentale **14**:165, 1864.

22. Fournier, A.: Syphilis héréditaire infiltrative gommeuse, Bull. et mém. Soc. méd. d. hôp. de Paris **2**:51, 1865.

23. Fuerth, L.: Lues congenita, Wien. med. Presse **6**:1214, 1865.

24. Lewin, G.: Die syphilitische Affection, Charité-Ann. **14**:210, 1868.

25. Ödmansson, E.: Abstr. from Danish in Virchow-Hirsch Jahresb. ü. d. Leistung. u. Fortschr. d. ges. Med. **4**:560, 1869.

26. Gueniot, M.: Ostéite suppuratif avec décollement, Gaz. d. hôp. de Paris **42**:61, 1869.

27. Wegner, G.: Ueber hereditäre Knochensyphilis, Virchows Arch. f. path. Anat. **50**:305, 1870.

28. Parrot, J. M.: Sur une pseudoparalysie causée par alteration du system osseux chez les nouveaux nés atteints de syphilis héréditaire, Arch. de physiol. **4**: 319, 470 and 613, 1871; Syphilis osseuse des nouveau-nés, Paris, 1873, vol. 48, p. 92.

i.e., a nutritional disturbance of the bone tissue at the point of ossification. Parrot was the first to declare that every bone of the skeleton of infants with congenital syphilis is affected, and a localization table of lesions was made by him which has stood the test of time. Wegner's material was largely fetal, while Parrot studied infants who had lived several weeks, and it was he who described the course of lesions of the bone. In addition, he studied osseous lesions of fetuses and established the fifth month of uterine life as the earliest time for the appearance of bone lesions.

Waldeyer and Köbner,[29] 1872, supplemented the investigations of Parrot and Wegner by finding microscopic evidence of epiphysial separation not demonstrable in gross specimens. They pointed out the specific character of the granulation tissue at the epiphysial borders.

The first discoverable American report is by Curtis Smith,[30] in 1872, of congenital dactylitis syphilitica. Oviously, the publications of his immediate predecessors were unknown to him. In the following year, Fränkel [31] emphasized that bone lesions are most pathognomonic of congenital syphilis.

In 1874, Poncet [32] published a pathologic study, and Henoch [33] contributed a clinical report.

In 1875 appeared the first important American publication in a book of 175 pages, by Taylor.[34] This book affords interesting reading today. Written long before the Wassermann test, the roentgen ray and the modern system of "follow up," he was able to report twelve cases of his own in addition to several others. He recognized clinically separation of the epiphyses and was able to follow up some cases until a "cure" was affected. He also believed that "prompt and vigorous treatment will avert such structural changes as would interfere with the future growth of bones." Taylor was in advance of his time in stating, that because an infant was born syphilitic and in late infancy developed rickets, it was not to be deduced that syphilis was the cause of the rickets. In this book he took issue with the celebrated Parrot, who fell into the error of stating that syphilis may be considered one of the causes of rickets. His publication deservedly received proper consideration

29. Waldeyer, K., and Köbner, L.: Beitrag zu hereditäre Knochensyphilis, Virchows Arch. f. path. Anat. **55**:367, 1872.

30. Smith, Curtis: A Case of Congenital Dactylitis Syphilitica, Am. J. Syph. & Dermat. **3**:33, 1872.

31. Fränkel, E.: Ueber placentar Syphilis, Arch. f. Gynäk. **5**:1, 1873.

32. Poncet, A.: Syphilis infantile, Bull. Soc. anat. de Paris **49**:118, 1874.

33. Henoch, E.: Klinisch Anatomie Befunde bei hereditäre Syphilis, Charité-Ann. **1**:616, 1874.

34. Taylor, R. W.: Syphilitic Lesions of the Osseous System, New York, William Wood & Company, 1875.

among European observers. In the same year, Birsch-Hirschfeld [35] presented a clinical report. In 1877, Howard [36] reported a case of epiphysial disease, and Macnamara,[37] of London, described a case of epiphysial and diaphysial hyperostoses. In 1878, Wiltshire [38] described epiphysial separation with secondary pyogenic infection of the joint.

The first large collection of syphilitic material was presented by Abelin [39] of Stockholm in 1879, it consisted of 215 syphilitic infants, 23 of whom showed osseous lesions. He was the first to emphasize that the lesions of the bone of acquired syphilis in early childhood simulated those of the adult and differed decidedly from the congenital form of the disease. In 1879, Parrot [39a] unfortunately promulgated the principle that "without hereditary syphilis there is no rickets." He apparently confused certain rachitic and syphilitic lesions, but without the aid of the roentgen ray, the Wassermann test and the chemical analysis of the blood it is surprising that he learned so much rather than that he made an error for which it would seem he has not yet been forgiven. He died before he had an opportunity to see the fallacy of this theory.

In 1880, Lees and Barlow [40] took issue with Parrot on certain phases of his thesis, but even they agreed that rickets might be caused by congenital syphilis on the basis of damaged nutrition. In an independent publication in the same year Barlow stated that epiphysial separation was not caused by suppuration in the softened osseous zone, although in the structures surrounding the end of the bone suppuration is occasionally seen. In the same year, Parker [41] published a clinical report.

In 1881, Heubner [42] clearly defined suppurative arthritis in congenital syphilis as due to secondary infection independent of the co-existing syphilitic process.

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35. Birsch-Hirschfeld, W.: Beiträge zu pathologische Anatomie der hereditäre Syphilis in Neugeborenen, Ztschr. f. Heilk. **16**:166, 1875.

36. Howard, W.: Epiphysial Diseases in Infantile Syphilis, Proc. Path. Soc. London, Lancet (May 5), 1877, p. 646.

37. Macnamara, C.: Syphilitic Disease of the Bone, Lancet **2**:833, 1877.

38. Wiltshire, W. H.: Diseases of the Joints, Brit. M. J. **1**:732, 1878.

39. Abelin, H. J., quoted by Hochsinger, C.: Studien ueber hereditäre Syphilis, Vienna, 1904, vol. 2, p. 37.

39a. Parrot, M. J.: Remarks on the Osseous Lesions of Hereditary Syphilis, Lancet **1**:696 and 703, 1879.

40. Lees, D. B., and Barlow, T.: On the Etiology of Craniotabes, Med. Gaz., 1880, part 2, p. 611.

41. Parker, R. W.: Remarks on a Case of Congenital Syphilis, Med. Times & Hosp. Gaz. **1**:145, 1879.

42. Heubner, R.: Beitrag zu Kenntnis der hereditäre syphilis, Virchows Arch. f. path. Anat. **84**:248, 1881.

In the same year, Pellizzari and Tafani [43] divided the pathologic process into two main types: (1) chondrocalcosis characterized by interference with the normal growth of bone and (2) specific inflammatory processes with subdivision of periosteal, osteoperiosteal and genuine gummatous processes.

In 1882, Stilling [44] made further studies of epiphysial separations, and was the first to describe their healing. In 1885, Dreyfous [45] published a case report and a review of the literature. In 1887, Lane [46] presented a case of multiple suppuration of the joints, but Hutchinson,[47] in discussion, pointed out the secondary pyogenic nature of the condition.

In 1886, Kassowitz and Hochsinger [48] demonstrated streptococci as the secondary invader, causing purulent arthritis in congenital osseous syphilis. In 1890, Fischer [49] reported a case of osteomyelitic and periostitic lesions.

In the decade between 1880 and 1890, many controversial articles were published regarding the point raised by Parrot and sustained by others regarding the relation between syphilis and rickets. In 1887, Cazin and Iscovesco [50] accurately described the anatomic difference between the two types of pathologic lesions and definitely demonstrated that the osteophyte, the decalcification and the substitution of the hard bony tissue by osteoid tissue are alien to syphilis and represent rickets. Nine years later, Heubner [51] sharply opposed the theories of the pathologic changes of the two diseases, stating that "while in rickets the changes consist of a delay in deposition of the inorganic ingredients of bone, in syphilis it is the organic substances which fail to form."

Even at the opening of this century the question was warmly debated, being supported by Kassowitz' stand that rickets is a con-

43. Pellizzari and Tafani: Malattie della ossa da sifilide creditaria, Firenze, successori Le Monnier, 1881.

44. Stilling, H.: Ueber die syphilitische Osteochondritis der Neugeborenen, Virchows Arch. f. path. Anat. **88**:509, 1882.

45. Dreyfous, F.: De la pseudoparalytique syphilitique maladie de Parrot, Rev. de méd. **5**:562 and 673, 1885.

46. Lane, E., quoted by Hutchinson, J.: Syphilis, London, Cassell & Company, 1887, p. 517.

47. Hutchinson, J.: Syphilis, London, Cassell & Comagy, 1887.

48. Kassowitz, M., and Hochsinger, C.: Ueber einen Microorganism in den Geweben kongenitaler syphilitische Kinder, Wien. med. Bl. **9**:1, 1886.

49. Fischer, T.: Zur Kasuistik der hereditäre Syphilis des Knochensystem, München. med. Wchnschr. **36**:110, 1890.

50. Cazin and Iscovesco: Des rapports du rachitis avec la syphilis, Arch. gén. de méd. **2**:257, 422 and 567, 1887.

51. Heubner, J. O. L.: Syphilis im Kindesalter, in Gerhardt: Handbuch der Kinderkrankheiten, Tübingen, H. Laubschen, 1896, suppl. 1, p. 307.

genital disease. It might be said that the conviction of the relationship between the two diseases was as Howland [52] described it in relation to the congenital origin of rickets, "The belief died with those who held it rather than that they themselves ever gave it up."

Pommer,[53] Tschistowitsch,[54] Schmidt,[55] Wieland,[56] Thomsen [57] and others ended the controversy by showing that the cases of so-called congenital rickets were really syphilitic.

In 1896, von Recklinghausen [58] reported before the Congress of Natural Scientists in Frankfurt on the nature of periostitic hyperostosis. According to him, the shale formation is due to compact bone deposition taking place in successive layers about the primary cortex, as a result of the constant periosteal proliferation. These layers obtain their great density after the acute stage of the productive periostitis is over and intensive calcification of the previously soft osteophytes begins.

CONTEMPORARY LITERATURE

In 1902, Schmidt [55] emphasized the epiphysial predilection over the diaphysial in osseous syphilis.

At the pediatric section of the German Congress of Natural Scientists in Aachen in 1900, Hochsinger [59] presented the first roentgen pictures of congenital osseous syphilis. In several publications during the following years he presented further roentgenologic observations, and in 1904, in his voluminous two volume work dealing with every phase of the disease, anatomic, clinical and roentgenologic, in great detail, he included a number of excellent roentgenograms. While his technic was primitive as compared with that of later roentgenologists, it enabled him to present a fairly complete description of the fundamental roentgen phenomena as found not only in the long bones, but also in the short hollow bones of the extremities. The emphasized principle of

52. Howland, J.: Etiology and Pathogenesis of Rickets, Medicine **2**:350 (Nov.) 1923.

53. Pommer, G.: Zur Kenntnis der hereditäre syphilis, Verhandl. d. deutsch. path. Gesellsch. **9**:312, 1905.

54. Tschistowitsch, T.: Zur Frage der kongenitaler Rachitis, Virchows Arch. f. path. Anat. **148**:140, 1897.

55. Schmidt, M. B.: Kritisches Referat über Knochenkrankheiten, Ergebn. d. allg. Path. u. path. Anat. **7**:262, 1902.

56. Wieland, E.: Ueber osteoid bei Foeten, Deutsche med. Wchnschr. **35**: 1520, 1909.

57. Thomsen, O., quoted by Schneider, P.: Ergebn. d. allg. Path. u. path. Anat. **20**:185, 1923-1924.

58. von Recklinghausen, W.: Case Reports to the Medical Society of Strassbourg; abstr., Wien. klin. Wchnschr. **9**:674, 1896.

59. Hochsinger, C.: Studien über hereditäre Syphilis, Vienna, Franz Deuticke, 1904, vols. 1 and 2.

Hochsinger's conceptions is that he did not consider the congenital syphilitic tissue products to be of a gummatous, neoplastic nature, but described them as diffuse, specific, inflammatory processes. This process manifests itself everywhere in the body where active growth predisposes the tissues to invasion by the virus. This is the developmental theory of Hochsinger. According to him, "epiphysiolysis" is always a real fracture, marking the site of greatest softening, and frequently depends on external circumstances rather than on the stage of the process. He found microscopic evidence of osteochondritis in all syphilitic fetuses. Between 1901 and 1910, a number of roentgenologists and pediatricians presented studies with increasingly better technic. Köhler,[60] 1901, Holzknecht and Kienboeck,[61] 1902, Thomsen,[62] 1907, and Reyer,[63] 1908, are the outstanding workers of this period. Oluf Thomsen [62] was the first to point out that the roentgen ray offers the best method of discovering congenital syphilis in new-born infants otherwise showing no evidence of the disease. In 1912, he published his complete study based on an imposing collection of 200 cases, many with autopsies and careful anatomic and bacteriologic investigations. He considered Wegner's three stages of the disease to be arbitrary and united the first and second stages into one stage, which is in contrast to the so-called third stage of granulation tissue that is usually stated to be the cause of epiphysial separation. He considered the main source of granulation tissue to be the periosteum. The "gummas" of Orth he believed are merely isolated foci of granulation tissue. He observed that periostitis is always found where granulation tissue develops. All cartilage preformed bone and even the centers of ossification are involved in the syphilitic process. He mentioned the tendency of osseous lesions to heal spontaneously. About this time the bacteriologic study of the disease was initiated by the discovery of spirochetes in the bone lesions by Levaditi and Sauvage [64] in 1905. A number of pathologic bacteriologic studies followed by Bertarelli,[65] Beitzke,[66] Verse [67] (1906),

60. Köhler, A.: Knochenerkrankungen im Roentgenbild, Munich, J. F. Bergmann, 1901.

61. Holzknecht and Kienboeck: Die osteochondritis syphilitica im Röntgenbild, Fortschr. a. d. Geb. d. Röntgenstrhlen. **4**:247, 1902.

62. Thomsen, Oluf: Abstr. from Danish in Jahrb. f. Kinderh. **66**:125, 1907.

63. Reyer, W.: Ueber Knochenveränderungen der hereditäre syphilis, Verhandl. d. deutsch. Röntg.-Gesellsch. **4**:115, 1908.

64. Levaditi and Sauvage: Sur un cas de syphilis héréditaire, etc., Compt. rend. Soc. de biol. **59**:374, 1905.

65. Bertarelli, E.: Spirochaeta pallida und osteochondritis, Zentralbl. f. Bacteriol. **41**:639, 1906.

66. Beitzke, H.: Ueber Spirochaeta pallida bei angeborener Syphilis, Berl. klin. Wchnschr. **6**:782, 1906.

67. Verse, M.: Die Spirochaeta pallida in Syphilis, Med. Klin. **6**:626, 1906.

Bab[68] (1907), Hoffman,[69] Hedren[70] (1908), Pasini[71] (1909) and Kohler[72] (1912), culminating in the well known work of Thomsen[67] in 1912, that of Löhe[73] in 1915 and that of Schneider[74] in 1921-1923.

ROENTGENOLOGIC INVESTIGATORS

Fränkel, Alexander and Wimberger have been the three oustanding roentgenologic investigators of the osseous lesions of the disease, and any presentation of the subject would be incomplete without acknowledgment of the influence their work has had on successive studies.

In 1911, Eugen Fränkel,[75] of Hamburg, published his well known monograph on the roentgenologic picture of the disease. His was the first systematic treatise devoted exclusively to this phase of the disease. In this work he pointed out the advantage of the roentgen method of approach, and emphasized that it permitted a perfect review of the skeleton in one plate. He stressed the interference with proper anatomic relationship by the trauma resulting from removal of a syphilitic bone from the body. He correlated his roentgen observations with examinations of pathologic material, and concluded that roentgenography is the method of choice for the investigation of this disease. In 1915, Bela Alexander,[76] of Budapest, approached the subject from the same angle in a work of great detail based on a limited selection of material, largely fetal. In this he offered an explanation for the co-existence of different stages of the disease in the same skeleton based on his serial examination of fetuses of different ages. He believed that the lesions made their appearance corresponding to the appearance of the zones of ossification of endochondral origin. Asymmetries in lesions he believed were caused

68. Bab, H.: Beitrag zur Bacteriologie der congenitalen Syphilis, München. med. Wchnschr. **54**:2265, 1907.

69. Hoffman, W.: Atlas der etiologischen experimentalen Syphilisforschung, Berlin, Julius Springer, 1908.

70. Hedren, G.: Spirochaeta pallida bei congenitalen Syphilis, Zentralbl. f. Bacteriol. **46**:232, 1908.

71. Pasini, N.: Spirochaeta pallida bei hereditäre Syphilis, etc., Ztschr. f. Stomatol. **7**:97, 1909.

72. Kohler, L.: Histologische Untersuchungen am congenitalen luetischen Zahnkeim, Deutsche Monatschr. f. Zahnh. **31**:47, 1913.

73. Löhe, B.: Klinische anatomische Untersuchungen ueber Skeletveraenderungen, Virchows Arch. f. path. Anat. **220**:95, 1915.

74. Schneider, P.: Die angeborene Frühsyphilis des Knochensystems, Virchows Arch. f. path Anat. **234**:95, 1921; Anatomie Roentgenologie Bacteriologie der angeborenen Syphilis, Ergebn. d. allg. Path. u. path. Anat. **20**:185, 1923-1924.

75. Fränkel, Eugene: Die angeborne Knochensyphilis im Roentgenbild, Fortschr. a. d. Geb. d. Röntgenstrallen, 1911, supplement, vol. 26.

76. Alexander, Bela: Die ostealen Veränderungen bei kongenitaler Syphilis, Leipzig, Johann Ambrosius Barth, 1915.

by asymmetric physiologic developments. He further demonstrated that periostitis in new-born infants is a persistence of fetal periostitis, which he believed did not exist without evidence of osteochondritis. He said that the so-called "coffin" formation of the shaft in periostitis was due to an elevation of the periosteum by a specific tissue that develops beneath it. He correctly emphasized that "epiphysiolysis" or epiphysial separation is a diaphysial event. To summarize: He took issue with Wegner's conception that the pathology is influenced by the length growth of the bones, and believed that it was dependent on the ossification process and receded when this was ended.

In 1925, Wimberger [77] in a notable study correlated the known pathologic observations with roentgenologic observations of his own. This was the first comprehensive article of a practical nature of value alike to the roentgenologist and the clinician. He divided osseous congenital syphilis into the following types: (1) fetal syphilis, (2) nursling syphilis, (3) recidive (period of relapse) period to about the fourth year and (4) syphilis tarda, beyond the fourth year. He observed that the earliest invasion of the osseous system is at the fifth or sixth month of intra-uterine life. The maximum changes in extra-uterine life are manifested in the first few months, rapidly decreasing beginning with the sixth month of life. Just how late nursling syphilis occurs he believed remains to be determined. From the second and third years the lesions take on the character of acquired infection.

Wimberger [77] correctly stated that the earliest degree of osteochondritis showing only slight widening of the preparatory zone of calcification is not accessible to roentgenologic investigation especially if the subchondral changes of the spongiosa are absent. In his opinion the first positive roentgenologic observations are unquestionable widening of the chalk shadow at the end of the shaft, "rarefactions or washed away appearance of the subchondral areas, or washed away appearance and irregular contour of the shaft end when preparatory chalk zone is altogether missing." In cases in which the changes are localized chiefly at the endochondral zone of ossification, the x-ray pictures show a wide horizontal shadow at the metaphysial end, which though it may look homogeneous and of equal thickness, on closer scrutiny may reveal difference as regards fullness and sharpness of border outlines, on one hand toward the epiphyses and on the other toward the spongiosa of the marrow space. The minimum found is a soft frayed outline. According to Wimberger, this picture, as found in fetuses and new-born infants, usually shows also a rarefied submetaphysial zone diaphysialward

77. Wimberger, H.: Klinisch-radiolische Diagnosis von Rachitis, Scorbut und Lues congenita, Ergebn. f. inn. Med. u. Kinderh. **28**:264, 1925.

of the shadow of the widened epiphysial border. Here the fine framework of the spongiosa is not closely attached to the narrow and clearcut line of the preparatory chalk zone, and the zone of the marrow spaces as seen in normal bones. Wimberger expressed the belief that it is easy to overlook such cases of skeletal syphilitic disease if periosteal changes are not manifest in the x-ray plate or the rarefied horizontal areas at the ends of the shaft are not marked.

He emphasized that according to roentgen observations, the widening of the shadow of the end of the shaft will recede parallel with the resorption phenomena in the metaphyses, i. e., with the appearance of rarefaction in the spongiosa. This also has been my experience.

In presenting the roentgen picture and the pathologic substratum of epiphysial separation, Wimberger sides with Kienbock and Fränkel and concluded that the separation is intrametaphysial and not epiphysial, although he acknowledged the possibility of real epiphysial separation as described by the older writers and more recently by Schneider. He pointed out that by the roentgen rays such epiphysial dislocation could be demonstrated only if an ossification center were present in the involved epiphyses, but that such centers are rarely present in the first few months of life, the elective age for osteochondritis, hence true epiphysial separation is not demonstrable by the roentgen rays even if present.

In the collection of pictures in this series my associates and I were enabled to demonstrate roentgenologically a true epiphysial separation (by a fortuitous circumstance) owing to the early appearance of the center of ossification. One can but agree with Wimberger that the break, except in rare instances, occurs in the ends of the shaft, but it may also occur through the metaphyses as well as on the epiphysial side of the metaphyses. The pathologic substratum for intrametaphysial breaks as offered by Wimberger [77] is that which has been accepted by numerous writers for a number of years. With increasing destruction by "gummatous granulation" in the metaphyses rarefaction increases, until finally the extreme end of the shaft, i. e., the preparatory zone of calcification, the recently deposited bone trabeculae with the cortex, is completely separated from the shaft itself by an irregular zone of rarefaction which extends the entire width of the shaft. Wimberger likened this process to the third stage of osteochondritis described by Wegner, and described the yellow or grayish-red gelatin-like layer which appears between the zone of calcification and the spongiosa. He described this as small cell infiltration and stated that it represents genuine gummatous tissue, causing resorption of lesser or greater parts of the preparatory calcification, as well as the youngest "boneshaft offshoots," leading thus to loosening of the metaphysial junction. The slightest trauma in the presence of

such severe structural changes causes a shift, an impaction or even a comminution of the disorganized framework at the endochondral zone of ossification.

One cannot agree that the so-called granulation tissue, whether it appears as an isolated focus, or is present in large amounts at the end of the bone or appears under the periosteum, could be properly called gummatous or a gumma. Roentgenologists and pathologists have tried too hard to think of and to write about congenital syphilis in terms of the secondary and tertiary lesions of acquired syphilis. I agree with Hochsinger,[59] "Es gibt keine sekundäre und keine tertiäre, es gibt nur eine congenitale Frühsyphilis." (There is no secondary or tertiary syphilis; there is only congenital early syphilis.) This refers only to infancy.)

As recently as 1928, Thomsen [78] supported Hochsinger and stated that the comparison of gummas of the third stage of acquired syphilis with the pathologic tissue of congenital syphilis is entirely incorrect. We had the opportunity of examining sections of bones which showed on x-ray plates isolated areas of complete rarefaction in the shaft and others which showed larger areas of rarefaction at the ends of the shaft, i. e., the most advanced forms of osteochondritis. In both the bone had been almost completely replaced by connective tissue which was soft, but which showed no evidence of necrosis. The tendency of the gummas of the bone in tertiary syphilis of adult , whether they occur in the flat bones or in the long bones, is to break down and discharge if long untreated. The opportunity was offered of examining 102 cases of osseous syphilis of congenital origin in early life, many of the severest type, and in no instance had any lesions discharged through the skin or showed evidence that the subcutaneous tissues were involved. We have had no experience with syphilis tarda as older children have not been available. One can agree with Herxheimer [79] that in general the younger the person the more diffuse the reaction, and as the organism grows older focal isolated tissue reactions become manifest, hence granulation becomes the rule. "Miliary syphilomata," a term Herxheimer borrowed from Schneider, is a primitive type reaction, a weak reaction to a severe infection; gumma is the strong local type of reaction, a strong reaction to a mild infection. Ekehorn [80] stated that vigorous reaction never occurs in congenital syphilis.

78. Thomsen, O.: Pathologisch anatomische Veränderungen über congenitale Syphilis beim Fetus und neugeborenen Kinde, Copenhagen, Levin & Munksgaard, 1928.

79. Herxheimer, G.: Die pathologische Anatomie der angeborenen Syphilis, Verhandl. deutsche path. Gesellsch., **23**:144, 1928.

80. Ekehorn, G.: Die Syphilitica vasculitis der Nabelgefaesse, Virchows Arch. f. path. Anat. **242**:93, 1923.

From his investigations of the large nodular lesions of congenital syphilis, Benda [81] concluded that one is dealing with structures essentially different from the gummas of acquired syphilis. These structures are characterized by processes typical of congenital syphilis, namely, interstitial productive inflammatory changes and miliary syphilomas. The secondary vascular changes taking place in these tumor structures differ fundamentally from the vascular changes arising in the development of gummas, in which these changes are closely related to the formation of "gummi" substance, and their ultimate fate is infarction and necrosis, which are never seen in syphilomas. Even in the exceptional cases in which the vascular changes seem largely to imitate those of gummas and the subsequent changes are somewhat similar, the process never advances to the extent seen in gummas. Benda [81] suggested the name "conglomerate syphilomas." While he did not wish to deny the possibility that genuine gummas do occur in congenital syphilis, he was much inclined to doubt it from his own experience.

Wimberger,[77] Löhe [78] and others called attention to the not infrequent roentgen appearance of two or more horizontal zones of rarefaction alternating with what appears to be a double zone of chalk grating or two widened zones of calcification. Since only two such roentgen examples have been seen, and since no opportunity to study the lesions pathologically has been presented, the explanation of others for the pathologic background will have to be discussed.

Schneider [82] stated that the possibility that the two layers of granulation tissue may represent subsequent attacks of the disease remains to be investigated. Schneider also pointed out that two layers of granulation tissue may arise from different sources, one in the manner described by M. B. Schmidt originating from the cartilage marrow canals and the other from the submetaphysial bone-marrow. Schneider stated that in the coalesced layers the persisting marrow spaces may produce new bone tissue of incomplete texture, and this new zone simulates a new chalk grating. Thus the roentgen picture shows a widened zone of provisional calcification; proximal to this is a zone of rarefaction, and diaphysialward is another zone of overdense bone and again proximally is a rarefied zone. It seems possible that the double zones are the result of beginning spontaneous involution followed by relapse, since it is generally known that the osseous lesions of congenital syphilis will sometimes heal spontaneously. In 1921, Shipley, Pearson and Weech [83]

81. Benda, H.: Die miliäre Syphilomen, Verhandl. d. deutsche path. Gesellsch. **23**:256, 1928.

82. Schneider, P.: Ueber die Organveränderungen bei de angeborenen Frühsyphilis, Verhandl. d. deutsche path. Gesellsch. **23**:177, 1928.

83. Shipley, P. G.; Pearson, J. W.; Weech, A. A., and Greene, C. H.: X-Ray Pictures of Bones in Diagnosis of Syphilis, Bull. Johns Hopkins Hosp. **31**:75, 1921.

examined 300 fetuses from the sixth month of intra-uterine life nearly to term. They noted that the beginning of the syphilitic process as shown by the roentgen rays is an intensification of the shadow cast by the bone at the epiphysial line.

It seems to form a cap on the end of the trabeculae of the spongiosa. This is significant of the beginning of abnormally heavy calcification of the provisional calcified bone. It must be remembered that while the provisional zone of calcification in the cartilage of the normal embryonic bone is relatively very narrow, in many cases only one or two cells deep, in the syphilitic bone the calcified cartilage may show on section a width of from 0.5 to 1.5 mm.

In 1927, Péhu and Chassard,[84] in describing osteochondritis, approached the subject in a novel fashion. They mentioned that the calcification zone of a normal infant is about 1 mm. wide, a bluish hyaline-like layer with its convexity toward the epiphyses from which it is separated by a whitish band 2 mm. in width. The three layers, as they termed them, "spongy substance, calcification zone and epiphysial band," are covered by yellow periosteum with an aponeurotic aspect, 1 mm. in thickness. Should one break the connections between the cartilage and shaft by a brisk knock, the surface of separation would be smooth and even. In osteochondritis, on the other hand, the connecting cartilage zone of calcification is irregular and of unequal thickness, its color has changed from blue to grayish yellow, and a forceful separation would yield a rough, uneven and dented surface. "To obtain a separation in osteochondritis between cartilage and zone of ossification one would have to apply greater force as chondro-metaphysial adhesions have been developed." This statement is misleading, since the chondrometaphysial adhesions that are present when the disease has advanced to the stage described by these authors are chiefly made up of tongues of brittle calcified ground substance that have invaded the cartilage along the blood vessels and tongue of columnar cartilage cells that have invaded the shaft, neither of which are as strong as the normal trabecular structure which in the normal bone is intimately attached to the epiphysial cartilage.

Pick[85] asserted that osteochondritis begins in intra-uterine life but in exceptional cases it may begin in the first few months of extra-uterine life in infants who showed no osseous lesions at birth. He contended that osteochondritis can occur in childhood and cited the case of a girl, aged 11 years, who came to autopsy. He expressed the belief that the pathologico-anatomic characteristic of this lesion consists in the forma-

84. Péhu, M., and Chassard, M.: Schéma nosologique des ostéopathies syphilitiques dans la première enfance, J. méd. franç. **16**:427, 1927.

85. Pick, L.: Ueber Osteochondritis syphilitica im Kindesalter, Verhandl. d. deutsche path. Gesellsch. **23**:248, 1928.

tion of large spirochete-free caseous gummata associated with strong reactive and restitutive sclerosis of the bone.

Herxheimer,[79] in commenting on the pathology of the "second stage" of osteochondritis, stated that it is definitely inflammatory as indicated by its cellular and mesenchyme proliferation; he admitted that mesenchyme proliferation may be due to stimulation caused by the damaging effect of the virus and its growth-disturbing nature, i. e., "osteochondritis passiva" with defective osteoblast formation. Herxheimer asserted that such lesions are not specific, but become so with demonstration of the spirochetes. He qualified this statement by stating that even in the absence of spirochetes these lesions are pathognomonic, as he knew of no other condition that might cause them. He quoted Virchow as saying, "In syphilis it is manifest that the morphology in itself has no absolute value; only by its development, by its regression, its life history does it obtain its significance."

After summarizing the concepts of the three roentgenologists who have added the most to the knowledge of osteochondritis, I shall now approach the purely pathologic interpretation as seen by Schmidt,[86] Schneider [87] and Thomsen,[88] the men who have contributed most to this phase of the disease.

PATHOLOGIC INVESTIGATORS

Schmidt, in a series of studies,[88] stated that the bony skeleton is the favorite tissue for spirochetal invasion and that organisms are most abundant in the tissues of active growth—the "cartilage marrow," the bone-marrow, the deep layers of the cartilage and the bone coverings, the perichondrium and the periosteum. Osteochondritis is never absent when syphilitic changes are found in the body, and it is frequently the sole manifestation of the disease. In growing bones the invaders may be found within the newly formed "bone bodies," where they are partly destroyed and partly survive to be freed by the later transformation of these bone bodies and then, as Schneider declared, may set up relapses. In recent invasion the distribution of the organism depends on the growth activity of the different parts, as in rickets; the greatest intensity is reached in the ribs, the long bones showing the greatest growth, namely, the upper and lower end of the femur and the bones of the leg, then the distal and proximal ends of the bones of the forearm and the proximal end of the humeri. The pelvis and scapula, particularly the

86. Schmidt, M. B.: Ueber Osteochondritis syphilitica, Verhandl. d. deutsche path. Gesellsch. 2:233, 1905; Knochenkrankheiten, in Aschoff: Pathologischen Anatomie, Jena, Gustav Fischer, 1923, vol. 2, p. 179; footnote 55.

87. Schneider (footnotes 74 and 82).

88. Thomsen (footnotes 57, 62 and 78).

former, were also found to be involved. Schmidt, as opposed to Wegner, described but two forms of osteochondritis, a reactive and a nonreactive form. In the latter, or first type, he expressed the feeling that the changes are due to damage of the osteoblastic tissues.

According to Schmidt, in the first or nonreactive form, the following changes may be present: "Widening of the zone of calcification, visible macroscopically as a whitish yellow line between bone and cartilage due to delay in the apposition of bony substance in the youngest marrow spaces, while the opening of the cartilage cell columns from the marrow side progresses in the usual manner." The zone consists of columns of ground substance of calcified cartilage having a lattice arrangement (the so-called chalk grating), in the meshes of which marrow tissue is present. The border of this zone is sharper toward the epiphyses than toward the diaphyses. This is usually associated with a widening of the layer of cartilage proliferation. Sometimes there is an absolute reduction in cartilage proliferation, leading to widening of the horizontal septum of the cartilage ground substance first described by Lentz [89] (the Lentz line). According to Wieland,[86] the earliest changes consist of normal cartilage absorption and normal bone apposition with persisting resorption and increased deposition of lime salts in the ground substance and in the cells of the zone of cartilage proliferation. As the lesion progresses, Schmidt maintained, there is "further widening of the zone of calcification, the border line toward the cartilage becomes irregular since lime salt deposition increases beyond the normal, running through the entire thickness of the hypertrophic zone, advancing up the cell columns in some places, absent in others, while especially about the larger cartilage vessels tongue-like protrusions reach out to the resting cartilage." The tonguelike protrusions toward the epiphyses correspond to the equally broadened extensions of the cartilage marrow canals through the proliferative layer.

Schmidt's [90] comment on the origin of the "granulation tissue" in the severe form of osteochondritis is one of the most interesting contributions to the subject of congenital osseous syphilis. In the second stage, or state of reaction, the third stage of Wegner, Schmidt concluded that the submetaphysial layer of connective tissue does not originate from bone-marrow of the diaphyses, and the trabeculae it surrounds are not residues of destroyed bone of endochondral origin. He stated that this layer of altogether foreign type of connective tissue, having in varying proportions the character of granulation tissue or that of tissue capable of metaplastic bone formation originates from the cartilage canals. Furthermore, the appearance of this granulation

89. Lentz, N.: Osteochondritis und Rachitis congenita, Diss., Göttingen, 1895.

90. Schmidt (footnote 86, first reference).

tissue, which he stated is the usual forerunner of epiphysial separation, does not appear in varying localizations but in one definite lawful site. One is not dealing with resorption of already formed bone, but with a defect of ossification within one layer of cartilage canals. In other words, owing to the syphilitic infection, the connective tissue in the cartilage canals proliferates most in those lying nearest to the diaphyses, i. e., between the proliferating and the resting cartilage; the proliferating tissue assumes the character of granulation tissue, hence the cartilage canals are widened and the contiguous ones become confluent.

The tissue proliferation does not penetrate into cartilage in a straight line but leaves irregular tongues of the cartilage standing. Thus lacunae appear in the ossification cartilage, which subsequently—with progress of marrow space formation—are surrounded and swallowed up into the zone of primary marrow spaces. This proliferative connective tissue, as well as its matrix, the perichondrium, and the enclosed residue of cartilage—possesses the capacity of metaplastic bone formation and if here and there a connection arises between this cartilage marrow and the bone marrow coming from the diaphysis, the cells of the latter may penetrate into the former and transform the cartilage marrow to a greater or lesser extent—into bone marrow, in the same manner as when cartilage columns are being normally transformed.

When infants remain alive for some weeks, further changes occur which obscure the picture: 1. Bone apposition progresses from the diaphyses in the youngest marrow spaces to the place where cartilage canals have become confluent. 2. Epiphysial cartilage is being reduced progressively by the proliferating cartilage marrow, this being particularly strong in canals descending into the zone of proliferation. The widening and the coalescence of the canals cause the zone of cartilage proliferation to disappear except for a few tonguelike segments. The pathologic connective tissue layer is bordered on one side by the ossified diaphyses and on the other by the epiphysial cartilage.

According to Schmidt, as a result of the preceding changes, epiphysial separation arises as follows: "Either the connection between the remaining communicating cartilage trabeculae is bent, leaving the epiphyses attached to the shaft only by connective tissue, or the proliferative connective tissue layer lifts itself from the underlying youngest marrow spaces which close up the diaphyses." According to Schmidt,[90] in epiphysial separation one is not dealing with a disease of the bone-marrow, since the entire process is part of a disease of the perichondrial connective tissue system. Turnbull [91] stated that fibrosis is seen microscopically in all but the slightest and earliest lesions. He noted that the fibrosis may affect the marrow of the metaphysis or of the canals in the

91. Turnbull, H. M.: Congenital Syphilitic Inflammation of the Long Bones, Lancet **1**:1239, 1922.

cartilage or both. "In advanced, intense inflammations, a dense granulation tissue is formed." He expressed the belief that in the metaphyses, formation of such granulation tissues is associated with erosion by osteoclasts of trabeculae of calcified cartilage and bone. Schmidt likened the changes in the bone to those of other tissues—pancreas, lung and liver—in which the connective tissue takes the upper hand in growth while the parenchyma is retarded. He expressed the opinion that there is a similarity in these organs and bones in the structure of the proliferating granulation tissue which varies between granulation tissue poor in cells capable of metaplastic bone production and definitely gummatous tissue with necrosis.

Schneider,[92] emphasized that local tissue reactions in bone lesions are actually due to the presence of the spirochete but he expressed the belief that there is no exact relation between spirochetes and tissue reaction. He did not agree with Verse,[67] who found that the spirochetes are present inversely in proportion to the severity of the lesion, but that when the intensity of the lesion is marked the greatest numbers of spirochetes are found, and that the lesions persist in their intensity longer than could be explained on the basis of the number of spirochetes. "The greater their number, the longer will they take to disappear." He divided osteochondritis into two forms. The first or passive form is characterized by a deficient bone deposition in the primary bone-marrow zone behind the epiphyses, while the vascular offshoots from the bone-marrow keep on pushing ahead, opening up and penetrating through the cartilage. The subepiphysial zone, the so-called primary bone-marrow zone, is deficient in bone deposition, while provisional calcification proceeds more rapidly than normally, thus causing a persistence of columns of cartilage ground substance between the vascular loops, the so-called chalk lattice, while the normally growing columns of spongiosa remain behind on account of the reduced osteoblastic activities. The three main characteristics of this form of osteochondritis are: (1) excessive cartilage calcification, (2) persistent chalk lattice and (3) deficient subchondral spongiosa formation. The last two he considered as caused by a disturbance of osteoblastic activity due, according to Waldeyer and Köbner,[89] to a greater or a lesser lack of osteoblastic cells. The next phenomenon is a disturbance in the growth of cartilage. Schneider also expressed the belief that exaggerated calcification may be due to hyperemia in the cartilage columns which appears to be a reaction to the spirochetes. With severe degrees of reaction there occurs a cellular increase in the cartilage cell columns as well as a twistlike new bone formation, coming earlier than usual, on the inside and on the walls of

92. Schneider (footnote 74, first reference).

the ascending branches of the cartilage cell columns. These columns displace the adjacent ground substance and also cause a chemical change in the contiguous ground substance in the form of increased staining capacity, thus giving an osteoid appearance.

Schneider maintained that the most delicate reaction to spirochetal invasion is manifested as a reduction of osteoblastic activity at the zone of ossification.

His conception of the late or active form of osteochondritis is similar to that of other authors; he believes, however, that the granulation tissue present in this state is not a specific tissue, but is the same as that which occurs in the liver, pancreas and other organs. He noted the presence in acute cases of abscess-like, miliary, leukocyte accumulations in the form of miliary syphilomas. He also noted the presence of small miliary foci of suppuration, which are never visible macroscopically. He further observed that in the areas softened by granulation tissue he had found the osteoblastic giant cell broken down or flattened out. He also found new bone formation within the granulation tissue, even while destruction is going on, but more especially during the healing process.

Regarding the histology, Schneider [82] agreed with M. B. Schmidt that the granulation tissue may also originate "from the cartilage marrow cells derived from the perichondrium." The cartilage cell columns in the presence of spirochetes and the excessive hyperemia go into reactive growth, greatly increasing their cellular elements, and soften out or liquefy the surrounding ground substance until they actually become confluent and the entire layer becomes granulation tissue. Simultaneously, there is a cessation of cartilage proliferation. Thomsen, on the other hand, contended that granulation tissue is derived from periosteal tissue.

In summarizing the two main types of lesions, one notes: The first, the chalk lattice-producing type, depending on damage to osteoblastic tissue production, he called passive osteochondritis. The second type, with the production of the characteristic granulation tissue, he called active osteochondritis. Schneider [82] did not think that the second stage is merely a subsequent stage of the first, but that it is essentially a different form of reaction depending rather on an age tendency to active reaction. He expressed the belief that this accounts for the different forms in intra-uterine and extra-uterine life.

Löhe [73] studied sixty cases of osseous congenital syphilis pathologically and with the roentgen rays, in many of which the patients lived several weeks. He divided his material into six groups. He emphasized the diagnostic value of the Lentz [80] line, described by Lentz as a horizontal dark line in histologic preparations due to intensive stain-

ing qualities, situated at the upper border of the zone of calcification. Microscopically, he stated that this corresponds to the widening and fraying of horizontal septums of the cartilage canals. As they approach this line, the cartilage cells become more and more flattened, until finally the appearance of the canal is altogether lost. Pendergrass and Bromer [93] recently presented the roentgenographic differential diagnosis between rickets, scurvy and syphilis, and stressed the importance of the roentgenogram in the diagnosis of the last named disease.

PERIOSTITIS

The studies relating to periostitis are less convincing than those concerning osteochondritis, owing to the relatively smaller amount of pathologic material. Infants with the most extensive periosteal lesions as evidenced by x-ray pictures are frequently in the healing stage of the disease; hence the paucity of autopsy material.

Discussion of the histopathologic substratum in the various types of periostitis seen in the roentgenogram is still vigorous among German pathologists; more recently the French have entered the field. The question as to whether periostitis generally speaking is more marked at the middle of the shaft or at the ends does not seem sufficiently important to record. That it occurs in intra-uterine as well as in extra-uterine life seems clearly established. In its earliest stages the lesion is of no interest to the roentgenologist, since, like the superiosteal hemorrhage in scurvy, it gives no indication of its presence until lime deposition has begun.

Schneider [74] distinguished three types of periostitis: (1) the early specific disease, "periostitis recens syphilitica," (2) the epiphysial periostitis of epiphysial separations, "periostitis callosa" and (3) the late periostitis of the shaft with regression—healing of the bone disease—"periostitis secundaria reparativa."

Parrot,[88] Wegner,[87] Hochsinger,[89] Alexander,[76] Thomsen [87] have given their version of diaphysial lesions. The last author expressed the belief that it is the periostitis from whence the inflammation of the marrow ensues, while Alexander [76] expressed the opinion that it is an extension of the disease into the depth and surface of the bone. Schneider [92] emphasized that the cambium layer of the periosteum over the entire shaft, but especially at the ossification groove, is a favorite site for the spirochete. He expressed the belief that periostitis is present in nearly all cases of osteochondritis, and that there are cases showing this lesion alone. In mild cases he described an abnormal thicken-

93. Pendergrass, E. P., and Bromer, R.: Congenital Bone Syphilis, Am. J. Roentgenol. **22**:1, 1929.

ing due chiefly to a proliferation of the cambium layer at the epiphysial border which consists of lymphoid infiltration with some leukocytes, especially about the vessels. He also noted "fibred cartilage new formation in the periosteum," and in severe cases with epiphysial separation he found hyaline cartilage. According to Schneider, the newly formed osteophytes are mostly calcified, with an incomplete and twistlike structure; in the mild forms, they run parallel with the axis of the bone; in severe cases perpendicularly with a fibrous marrow layer separating them from the old bone. Restitution by way of lamellated bone is a later phenomenon. Schneider explained periostitis callosa as a compensatory process for the vanished cortex. He stated that in the granulation tissue-forming cases of osteochondritis with increasing rarefaction of the old cortex he found abundant periosteal osteophyte formation, which is not due so much to local specific irritation, as it contains but few spirochetes; it was previously recognized by Kassowitz as a reparative process limited to the epiphysial end of the diaphyses.

Schneider properly credited Fränkel as being the first to recognize that "periostitis secondaria reparativa" increases as osteochondritis recedes under therapy. One might add that it recedes either spontaneously or as a result of therapy. Hotz [94] had the same view as Fränkel.[78] Schneider [82] has seen ossifying periostitis spread over the entire shaft in older infants without osteochondritis in which residues of the spirochete containing "bone bodies" indicated the past disease. He stated that this late periostitis shows higher forms of organization. The twistlike bone is replaced by lamellated bone and the "fibred marrow between the beams" is penetrated by bone-marrow cells; medullization thus takes place. Simultaneously, the bone beams are restored and incorporated into the structure of the old cortex.

Péhu, in a series of articles with different collaborators,[95] has written extensively on osseous congenital syphilis. It would seem that in certain of his pathologic studies he might have confused syphilis with some other condition, possibly osteogenesis imperfecta or rickets, as he speaks of a fragility of the bones resulting in multiple spontaneous fractures of the long bones without osteochondritis.

94. Hotz, A.: Die Heilung der kongenitalen Knochensyphilis im Röntgenbild, Cor.-Bl. f. Schweiz. Aerzte **48**:631, 1918.

95. Péhu, M., and Enselme, J.: Sur la syphilis congénitale des os longs dans la première enfance, Rev. franç. de pédiat. **1**:261, 1925; Quelques radiographs des lésions osséous syphilis héréditaire, Lyon méd. **134**:621, 1924. Péhu, M.; Chassard, M., and Enselme, J.: Étude radiologique de la syphilis congénitale, etc., J. de radiol. et d'électrol. **10**:54, 1926. Péhu, M., and Policard, A.: Les raréfactions osseuses diaphysaires (Périositié ossifiante), Rev. franç. de pédiat. **3**:137, 1927. Péhu and Chassard (foonote 84).

Péhu [96] stressed the resemblance between certain types of periostitis due to syphilis and rachitic thickening of the shaft of the bone. Histologically, he believed that periostitis consists of two essential processes: "bone resorption causing rarefaction and bone new formation generally of a very early embryonic imperfect type." He pointed out that rarefaction is the predominant phenomenon. Within the compact bone of the cortical layer are found areas filled out by a highly vascularized connective tissue. He expressed the belief that the solid haversian tissue undergoes secondary rarefaction and the connective tissue spaces represent previously bony areas which become connective tissue after resorption of their lime. On this rarefied portion a superimposed new bone, embryonic in type, is formed, occurring in lamellated plates and resembling those formed in the calluses of fractures. He is satisfied that periostitis ossificans is explained by the co-existence of rarefaction and new bone formation. He called it anatomic hypertrophy and histologic atrophy and suggested the term hypertrophic osteoporosis as a better term than periostitis. One can but sympathize with Péhu and Policard in their concluding sentence: "One finds himself before a series of great problems of the pathogenic mechanism of congenital lues which still await their solution."

Péhu and Chassard [84] maintained that the so-termed "periostitis ossificans" is the result of a profound disturbance of osteogenesis, but that the nomenclature is incorrect since the periosteum itself is entirely normal.

Von Recklinghausen [58] reported two cases before the medical Society of Strassburg, 1896. In both a diffuse ossifying periostitis was present in the long bones of the extremities which were surrounded by several homogeneously developed layers of bone shales, without any evidence of sequestration in the coffined diaphyses. One patient, aged 10 years, also had carious foci of the cranium and spine. The other was an infant, aged 3 months, who still showed some residue of osteochondritis and osteomyelitis in addition to epiphysial separations.

Although these two cases were undoubtedly syphilitic, von Recklinghausen did not mean to infer that all long bones showing "periosteal cloaking" are syphilitic, yet his belief seems to be held by many who have read only the reference to his original case report. The most marked "periosteal cloaking" or "coffin formation" seen by us occurred in a rapidly healing severe case of rickets in a Negro child, aged 17 months. In this case the periosteal thickening was uniformly distributed over the long bones. Even in the presence of a positive Wassermann reaction one must be extremely careful lest rickets be

96. Péhu and Policard (footnote 95, fourth reference).

confused with syphilis, unless some other confirmatory lesion is present in association with periosteal cloaking. Rachitic cloaking tends to envelop both ends of the bone and the entire shaft and is uniformly distributed over all the long bones, while syphilitic cloaking is considerably less uniformly distributed and tends to involve more heavily either the upper or the lower half of the shaft. Lindsay, Rice and Selinger,[97] in a study of ninety-four patients with congenital syphilis of whom all but nine were negroes, found that in very young infants productive periostitis was the most common lesion.

97. Lindsay, J. W.; Rice, E. C., and Selinger, M. A.: Bone Changes in Congenital Syphilis, Am. J. Syph. **11**:118, 1927.

WHEEZING RESPIRATION IN CHILDREN

BRONCHOSCOPIC OBSERVATIONS ON STRIDOROUS AND ASTHMATOID BREATHING *

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PHILADELPHIA

The wheezing to which the observations that are to follow refer is that heard at the open mouth of the patient, not by auscultation through the wall of the chest.

When in a child the lumen of every air passage is of normal area in cross-section, the child breathes so quietly that either a very close approach or the observation of movements is necessary to make certain that the child is breathing at all.

To produce a wheezing audible without auscultation, the lumen of the airway must be encroached on by tissues, secretions or a foreign substance. The wheezing may be described as rattling, bubbling, crowing, harsh, whistling, vibratory, stridorous or merely noisy. The sound may be heard on inspiration or on expiration or on both.

The character of the obstruction to the free noiseless passage of air can be determined in practically every case by tripartite conference of the pediatrician, who can tap, look and listen on the outside, the roentgenologist, who can look through the patient, and the broncho-esophagoscopist, who can look inside the patient.

CONDITIONS IN WHICH WHEEZING RESPIRATION OCCURS

Compression Stenosis.—Compression stenosis may be due to any structure or foreign body outside the tracheal or bronchial wall.

A foreign body in the esophagus, as mentioned elsewhere in this paper, may compress the trachea by its bulk or by the secondary swelling or by both.

Thymic compression stenosis causes a wheezing well known to all pediatricians. Twenty years ago, John Boyce and I bronchoscopically demonstrated thymic compression stenosis in the living patient, disproving the arbitrary dictum of Friedleben that such a condition did not exist and was impossible.

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* Abstract of remarks made in connection with a chalk, lantern and moving picture demonstration at the meeting of the Central States Pediatric Society, Pittsburgh, Oct. 27, 1928.

Substernal goiter, sometimes congenital, is not so common a cause of compression stenosis and wheezing in children as thymic compression, but we have had a number of cases of this kind at the bronchoscopic clinic.

Adenopathy is relatively common in our records as having caused a wheeze mistaken for asthma. The most common site is at the bifurcation of the trachea. Either the right or the left bronchial orifice or both orifices may be occluded.

Bronchial Obstruction.—In considering bronchial stenosis due to compression, secretions or any other cause it is well to remember that there are three types of bronchial obstruction: (1) by-pass obstruction, air passes in and out but in diminished amount; (2) check-valve obstruction, air can pass one way only, either in or out; and (3) stop-valve obstruction, the air cannot pass either in or out.[1] Check-valve obstruction produces either emphysema or atelectasis, according to which way the check-valve is set; and a wheeze audible at the mouth may accompany either condition. The peculiarity of the obstructive emphysema is that though the breath sounds are distant or absent the percussion note is normal or hyperresonant. Diagnosis of the endobronchial cause can be determined only with the bronchoscope.

Cicatricial Stenosis.—Cicatricial stenosis as a cause of wheezing respiration was found in a number of our cases. Until the bronchoscopic examination revealed the actual condition, the wheeze usually led to an erroneous inferential diagnosis of asthma. The cause of the cicatricial stenosis was not always clear. In some instances, it was due to the suppurating through of a mediastinal gland. In other cases, it was due to the prolonged sojourn of a foreign body. In a few cases, there had evidently been a prolonged suppuration, abscess or bronchiectasis. Syphilis and tuberculosis were each found to have been the cause of a previous suppurative condition; but an acute infection seems more frequently to have been the cause.

Foreign Bodies in the Air and Food Passages.—Foreign Body in the Air Passages: One of the most important diagnostic signs of foreign body in the tracheobronchial tree is a wheezing heard at the open mouth. If a child has choked and gagged and this is followed by a wheeze it is absolutely certain that there is a foreign body lodged

1. Jackson, Chevalier: A New Diagnostic Sign of Foreign Body in Trachea or Bronchi, the "Asthmatoid Wheeze," Am. J. M. Sc. **156**:625 (Nov.) 1918. Jackson, Chevalier; and Lee, W. E.: Acute Massive Collapse of the Lung, Ann. Surg. **82**:364, 1925; Tr. Am. S. A., **43**:723, 1925. Jackson, Chevalier: Endothelioma of the Right Bronchus Removed by Peroral Bronchoscopy, Am. J. M. Sc. **153**:371, 1917; Bronchoscopy and Esophagoscopy, ed. 2, Philadelphia, W. B. Saunders Company, 1927.

somewhere. If the wheeze disappears, its disappearance is more often due to the foreign body having gone deeper into the bronchi than to expulsion of the intruder.

Foreign Body in the Esophagus: Many patients with supposed asthma have come to the clinic wheezing because of a foreign body in the esophagus. The obstruction to the lumen of the airway may be by compression due (1) to the bulk of the foreign body, (2) to the compressive swelling around the foreign body, (3) to laryngotracheitis and subglottic edema from overflow of food or secretion or (4) to ulceration of the tissue in which the foreign body is lodged, through the common wall, from the esophagus into the trachea. A number of patients, after prolonged treatment for supposed asthma, have come to the clinic and have been found to be suffering from foreign body, the removal of which promptly cured them of the wheeze.

Subglottic Laryngitis.—Acute infective laryngotracheitis is often a cause of wheezing and dyspnea. In the acute cases, it symptomatically resembles diphtheria, but in the residual chronic form associated with chronic subglottic edema it has produced a wheeze mistaken for that of asthma.

Papillomas.—Asthma was the erroneous diagnosis in twenty-seven cases of wheezing due to papillomas. In some of the cases, the papillomas were in the trachea, but more often they were in the larynx.

Pulmonary Abscess.—Thick pus in the bronchi in some patients produces a wheeze simulating that of asthma. In many such cases, bronchoscopic aspiration and inspection have entirely eliminated any element that could possibly be called asthmatic. In some instances, after the pus was aspirated, granulations obstructing the bronchi produced a pronounced wheeze. In some cases, cicatricial stenosis from healed areas was a factor in the production of the sound.

Bronchiectasis.—What has just been said of pulmonary abscess is equally true of bronchiectasis.

Asthma.—Asthma is placed last on the list, not because it is the least frequent, but because it is desired to emphasize the bronchoscopic point of view that it should be the last diagnosis to be reached. All the experience of the bronchoscopic clinic goes to show that the diagnosis of asthma should not be made until all other possible causes of wheezing have been excluded. I may be biased, but I feel that this can be done with certainty only by objective examination of the airway. All other diagnostic methods should be preliminaries to the bronchoscopy.

"All is not asthma that wheezes" is an aphorism that I think should be inculcated into every medical student, so that in his after-life he will

be on the alert for the causes of wheezing that not only are often serious and fatal if overlooked, but are quickly and easily curable if discovered.

Bronchoscopic Appearance in Asthma: There is no bronchoscopic evidence of spasm of the bronchi in asthma or in any other disease. By this it is not meant that no spasm exists in asthma, but simply that bronchoscopic examination during an attack of asthma affords no objective evidence of spasmodic contraction of the bronchi. I cannot say that no spasm occurs in the minute peripheral bronchi into which the bronchoscopist cannot look; but if spasmodic contraction occurs there in asthma, as a physicist I cannot understand why a wheeze audible at the mouth should be produced thereby, nor why bronchoscopic aspiration should stop the wheeze. On the other hand, pathologic states of the mucosa and pathologic secretions are the rule in all cases.

The most frequent pathologic condition found is a clogging of the bronchial orifice or bronchial lumen with pus or mucopus. The mucosa during an attack is, in many instances, red or crimson; sometimes it is livid or cyanotic; it is always congested.

The Secretion in Asthma: The secretion in asthma is typical. It is thick and tenacious; it requires strong negative pressure to pull it out. It is obviously the cause of the wheezing and coughing and of the patient's distress. When it is bronchoscopically aspirated, the patient is relieved until it reaccumulates. It clogs the cilia, and the cilia and the cough combined cannot expel it. In cases at the bronchoscopic clinic, Dr. John Kolmer has shown that the intense viscosity of the pus resulting in massive coagulation of the pus is due to an excess of fibrin. This is secondary to an excess of fibrinogen derived in excess from the blood during passive congestion.[2] What causes the passive congestion I do not know, but hundreds of cases at the bronchoscopic clinic afford evidence as to this kind of secretion being the cause of the wheeze, the dyspnea and all the other respiratory symptoms of asthma. Moreover, bronchoscopic aspiration causes both the wheeze and the dyspnea to disappear.

CONCLUSIONS

1. All is not asthma that wheezes.

2. If a patient presents a wheeze, there is always some obstruction in the larger air passages.

3. Most often a foreign body is the cause of the obstruction; next in frequency is a secretion difficult of bechic expulsion.

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2. Jackson, Chevalier: Bronchoscopy, Past, Present and Future, New England M. J. **199**:759, 1928.

4. Obstruction in the smaller bronchi does not cause wheezing audible at the open mouth.

5. Bronchoscopic examination practically always reveals the mechanical cause of wheezing.

6. Cooperation of the pediatrician, who can tap, look and listen on the outside, the roentgenologist, who can look through, and the broncho-esophagoscopist, who can look inside the patient, usually solves all diagnostic problems in which pulmonary symptoms are concerned.

Pediatric Biographies

WILLIAM HEBERDEN, THE YOUNGER
1767–1845

JOHN RUHRÄH, M.D.
BALTIMORE

William Heberden, the younger, who was the second but only surviving son of William Heberden, the elder, was born in Cecil Street on March 23, 1767. His early education was received at the Charterhouse and at St. Johns College, Cambridge, of which he was a Fellow. He was a brilliant student and carried many of the coveted student honors. He received his A.B. in 1788 and his A.M. in 1791; he was incorporated on that degree as a member of Christ Church at Oxford. He received his M.B. in 1792 and his M.D. in 1795. He was admitted as a candidate of the College of Physicians in 1795; he was a Fellow in 1796, and censor in 1799 and 1808, Harveian orator in 1809, and Elect in 1823 in place of Dr. Baillie, deceased. All of these data are recorded by Munk in his Roll of the Royal College of Physicians. He was also a member of the Royal Society.

The younger Heberden was a worthy son of his distinguished father and, like him, a classic scholar of wide learning. He rose rapidly in the medical profession and occupied an enviable position in the social world. He was made a physician to St. George's Hospital in 1793, but resigned in 1803. In 1795, he was made physician extraordinary to the Queen, and to the King in 1805. The following year he was made physician in ordinary to the Queen and in 1809 to the King. On several occasions George III offered him a baronetcy with a pension, but this was always declined. In 1812 his wife died, and he was left with nine young children. He retired from practice except for his attendance at Windsor Castle, and devoted the remainder of his years to the care of his children. He wrote "A Dialogue after the Manner of Cicero's Philosophical Disquisitions," which was published in 1818, and he also translated Plutarch on "Brotherly Love," which was dedicated to his children. In 1826, he returned to London to help his son who had started to study medicine, but the death of this son two years later from a dissection wound, and of another son and daughter subsequently, led him to devote the remainder of his life to the scripture and religion. In 1830, he published his "Reflections on the Gospel of St. John"; in 1836, a translation of the "Catholic Epistles" and in 1839,

a translation and commentary on the whole of the Apostolic Epistles and the Book of Revelation.

His medical works consisted of "Observations on the Increase and Decrease of Different Diseases, Particularly of the Plague" in 1801, and "Commentaries on the History and Cure of Disease," 1802, a trans-

MORBORUM PUERILIUM

EPITOME

AUCTORE

GULIELMO HEBERDEN

REGI REGINÆQUE BRITANNIARUM

MEDICO EXTRAORDINARIO.

LONDINI:

TYPIS S. HAMILTON, SHOE-LANE, FLEET-STREET;

VENEUNT APUD T. PAYNE, MEWS-GATE.

1804

Title page of "Morborum Puerilium Epitome"

lation of his father's celebrated work. In 1804, he published "Morborum Puerilium Epitome," which was translated into English the following year by J. Smith. In 1807, Heberden published his own translation which starts with the following explanation:

The following Translation of my Epitome Morborum Puerilium has been made at the request of several of my friends, who persuaded me that it would

be acceptable to the public. And it is proper to notice, which I do with some reluctance, that I have been the more ready to comply with their wishes, in consequence of a very different translation having already appeared by another hand, in which the sense of the original has been in many instances imperfectly rendered, and in some totally misrepresented.

This little book is one of the gems of pediatric literature and is reprinted in its entirety in "Pediatrics of the Past." No pediatrician should fail to read it. It is a model of brevity and succintness as well as clarity. It considers the more common diseases of children, preceded by a chapter on the diet and management of children, which may be quoted in part as an example of the style of the book:

ON THE DIET AND MANAGEMENT OF CHILDREN

It is always desirable, as far as we are able, to prevent diseases rather than to cure them; to obviate their causes rather than to remove their effects. And this is particularly the case with regard to children. We see other people broken down with luxury and intemperance, worn with care, or enervated by indolence; whence they become at once more liable to sickness, and are less easily restored. But the treatment of children is much more simple.

> They never supt in solemn state,
> Nor undigested feasts did urge their fate,
> Nor day to night luxuriously did join,
> Nor surfeited the rich Campanian wine.
>
> *Dryden, Georg. 3.*

But if the frail and helpless condition of infants demand a nice attention; if man be ushered into the world full of infirmities and wants; yet are we all born with a certain spring of vitality, a self-restoring power, which though sometimes disordered and oppressed, does neither require, nor bear, the administration of many remedies. Let then art take example from nature, and follow in her steps. Let all tight bandages be removed; let all superfluous food be withheld; that the play and growth of the limbs be unrestrained; and that the stomach may not be overloaded, nor the digestion impeded. What distortion of the limbs, what bad shapes have we to deplore from the former of these causes! On the other hand, what multiplied evils arise from indigestion! Sometimes there occurs vomiting, sometimes distension, sometimes griping, and very frequently acidities. It is doubtful whether we may not often attribute to the same origin likewise, the thrush, worms, wakefulness, pining, weakness, eruptions, and convulsions, to all of which children are especially subject. But when we observe that milk is the sustenance naturally provided for infants in the breast of their mother; why should not the food which is artificially prepared be made to bear some near resemblance to this, which we are sure must be proper for them? For what can anyone hope to effect by the most elaborate combination of drugs, while every day is furnishing fresh matter for disease? In fact, I am persuaded the health of children may best be consulted, not by the daily invention of new remedies; but by a careful management, and prudent regulation of their diet, so as to preclude the most usual sources of their disorders.

News and Comment

GENERAL

Annual Meeting of American Orthopsychiatric Association.—The eighth annual meeting of the Association will be held at the Hotel Pennsylvania, New York, Feb. 20 to 21, 1931.

Children's Division of Bellevue Hospital Transferred to New York University.—The Children's Medical Division of Bellevue Hospital, with practically the entire staff of the service, was transferred from Columbia University to New York University on July 1. This service has an average of about 140 patients. There are 6 wards, 1 each for the following groups: infants with infections; infants without infections; acutely ill older children; 1 each for boys and girls with chronic or subacute illness, and 1 for gonococcal infection complicated by other illness. A special ward for tuberculosis is under construction. Every bed is in a cubicle. In the near future the outpatient department will move into a new modern building with ample room for the large attendance. Most of the teaching of pediatrics will be done on this service with some courses at the City Hospital, Roosevelt Hospital and the Willard Parker Hospital for Contagious Diseases. The department has been reorganized with Dr. Charles Hendee Smith as professor of pediatrics and director of the Children's Medical Division.

Boston Hospital to Study Rheumatic Fever.—The House of the Good Samaritan, Boston, seeks $500,000 for an intensive study of rheumatic fever; in one month it has secured about $120,000 for the project. For seventy years the hospital has cared for needy women and children requiring prolonged treatment. It plans to build a wing for research, with Dr. T. Duckett Jones in charge of the work. Thorvald S. Ross, 100 Franklin Street, Boston, is treasurer of the fund.

Conference on Sight Conservation.—During a recent conference of the National Society for the Prevention of Blindness, held jointly with the National Organization for Public Health Nursing, special discussions were held on the conservation of vision in school children. It was reported that 1,000 school children in New York City had seriously defective vision and had failed to receive the attention that their handicap required. A request for 19 additional sight-saving classes had been made, but the board of education had been unable to meet this request on the ground of retrenchment, creating in the waiting list of 1,000 pupils a feeling of inferiority. There are now 79 sight-saving classes in New York City, accommodating 1,450 pupils, many of them in the elementary grades. There is urgent need for 21 additional classes in the elementary grades, and for 29 classes in the junior and senior high schools. Dr. Jules L. Blumenthal, director of the city bureau of child hygiene, said that the health department in its eleven clinics had examined 16,256 children in 1929, and that 10,905 prescriptions for glasses had been written.

Behavior Clinic in New York.—An appropriation of $100,000 has been approved by the board of estimates of the public school system of New York for the establishment of a behavior clinic. The purpose of this clinic is to study and help adjust cases of retarded, maladjusted, truant and otherwise delinquent children. There will be two units: a centrally located clinic for older children, and a branch to study preventive measures among younger pupils. Both branches will be under the supervision of a psychiatrist, aided by a pediatrician, case workers and psychologists.

Prof. Morquio Honorary President of Pan-American Congress.—At the sixth Pan-American Pediatric Congress at Lima, Peru, recently, Professor Morquio of Montevideo, Uruguay, was elected Honorary President.

Medal Given Dr. Arturo Aballi.—The Medical School of Havana and the Medical Federation of Cuba have given to Dr. Arturo Aballi, Professor of Pediatrics in the Faculty of Medicine in Havana, a gold medal in recognition of his services to Cuban medicine in general and pediatrics in particular. Dr. Aballi is a corresponding member of the American Pediatric Society and was the guest a few years ago, of the Section on Diseases of Children of the American Medical Association.

UNIVERSITY NEWS

Harvard Medical School announces the appointment of Dr. Stewart Hilton Clifford and Dr. Harvey Spencer as assistants in pediatrics and child hygiene.

BEQUESTS

The Children's Memorial Hospital, Chicago, was given $200,000 by the will of the late Thomas D. Jones.

The New York Orthopedic Hospital, New York, received $50,000 by the will of the late Marion Borden, Middletown, N. Y.

Abstracts from Current Literature

Pathology, Bacteriology and Biochemistry

Blood Calcium Distribution in Anaphylaxis in the Guinea-Pig. H. Brown and S. G. Ramsdell, J. Exper. Med. **49**:705 (May) 1929.

The total serum calcium is unchanged in anaphylactic shock. The membrane-diffusible fraction of the calcium is increased in animals showing the characteristic symptoms of anaphylactic shock when compared with sensitized animals not showing symptoms of shock or with normal controls.

Kugelmass, New York.

The Upper Respiratory Flora of Infants. Yale Kneeland, Jr., J. Exper. Med. **51**:617, 1930.

The upper respiratory tract is sterile at birth. In the first two weeks of life the infant acquires a basal flora comparable to that of adults except that the potential pathogens are absent. During the ensuing months the potential pathogens may appear without giving rise to symptoms, and by eight months the infant's flora is entirely comparable to the adult's. There is no evidence of a specific bacterial incitant for the first colds of infancy. In infants with recurrent colds, secondary infection of the nose with pneumococci or *Bacillus pfeifferi* probably plays a part.

Author's Summary.

Experiments with the Virus of Poliomyelitis. Richard Thompson, J. Exper. Med. **51**:777, 1930.

Efforts to adapt the virus of poliomyelitis to the rabbit organism and to produce poliomyelitis in rabbits by testicular injection and by injection into the brain after testicular passage produced no evidence that the virus could be adapted in this manner. Suggestive symptoms produced in very young rabbits were duplicated in nonspecifically treated and in uninoculated controls. The mixture of a vaccine virus, adapted to the rabbit organism, with the poliomyelitis virus in similar injections and passages did not aid the adaptation. The virus of poliomyelitis did not survive twenty-four hours in the rabbit testicle, either alone or mixed with vaccine virus. Repeated intraperitoneal and intradermal injection of poliomyelitis virus and of poliomyelitis and vaccinia virus mixtures did not produce the disease in rabbits. Massive doses of concentrated virus by stomach tube in conjunction with meningeal irriation did not produce symptoms in rabbits. No neutralizing substances against poliomyelitis virus could be produced in rabbits by the repeated intraperitoneal and intradermal injection of poliomyelitis virus or of poliomyelitis-vaccinia virus mixtures. Although attempts to infect monkeys by intrastomachic injections, after irritation of the mucosa with bile, were entirely negative, evidence was obtained that repeated intrastomachic injection after irritation with bile may produce an appreciable degree of immunity. No evidence could be obtained that the cellular elements of the blood contain the virus in any greater proportion than does the whole blood. One attempt to immunize by neutral virus-serum mixtures was entirely negative.

Author's Summary.

Centrifuge Experiments with the Virus of Vaccinia. F. F. Tang, J. Exper. Med. **51**:859, 1930.

Centrifuge experiments have been carried out with cell-free, active filtrates of vaccinia virus. The experiments have shown that the virus can be concentrated

by this method, even in filtrates that have been subjected to prolonged preliminary centrifugalization to throw down any inert particles that may have been present in the original filtrate. This fact, together with the knowledge that the virus can be almost completely held back by the Berkefeld N filter, as reported previously, indicates that the virus may be of considerable size.

AUTHOR'S SUMMARY.

THE EPIDEMIOLOGY OF SPECIFIC INFECTIOUS CYSTITIS AND PYELONEPHRITIS OF COWS. F. S. JONES and RALPH B. LITTLE, J. Exper. Med. **51**:909, 1930.

Bacteriologic examination of the genito-urinary tract of calves originating in a herd in which infectious cystitis and pyelonephritis existed among the cows revealed a variety of cultural types of diphtheroids. Of these types, one obtained from a considerable number of the calves resembled in morphology and cultural characters the organisms cultivated from animals with the disease. This group had agglutination affinities like those of the organism mentioned and was capable of absorbing agglutinin from antiserum specific for it. When three cows were inoculated intra-urethrally with cultures isolated from the sheaths of calves, transient infections developed in two, and severe prolonged cystitis and pyelonephritis in the third.

AUTHORS' SUMMARY.

RISE IN TEMPERATURE PRECEDING THE SYMPTOMS IN EXPERIMENTAL POLIOMYELITIS. S. D. KRAMER, K. H. HENDRIE and W. L. AYCOCK, J. Exper. Med. **51**:933, 1930.

The data presented in this paper offer a means of early recognition of experimental poliomyelitis in the monkey. The early appearance of the rise in temperature (from one to three days before the onset of the usual recognizable symptoms) associated with changes in the spinal fluid suggests that there is a stage in the experimental disease that corresponds to preparalytic poliomyelitis in the human being.

AUTHORS' SUMMARY.

THE ABSENCE OF SEASONAL CHANGE IN THE TOXIN-PRODUCING CAPACITY OF THE DIPHTHERIA BACILLUS. ARTHUR LOCKE and E. R. MAIN, J. Infect. Dis. **46**:514, 1930.

The toxin production of the Park 8 strain of the diphtheria bacillus was observed, under controlled conditions, for one year. At no time during that interval was there any indication of a significant seasonal fluctuation in the amount of toxin produced.

The seasonal variations in yield occasionally encountered in the large scale preparation of diphtheria toxin may be the result of failure to control completely the composition of the culture medium used, or of failure to use a unit of titration, such as the flocculation unit, which is independent of seasonal fluctuations in animal resistance.

AUTHORS' SUMMARY.

THE HEAT RESISTANCE OF THE VIRUS OF POLIOMYELITIS. H. J. SHAUGHNESSY, P. H. HARMON and F. B. GORDON, J. Prev. Med. **4**:149, 1930.

The exact thermal inactivation point of the virus of poliomyelitis apparently cannot be determined at the present time because there is no accurate method for standardizing the potency of virus preparations. The results reported suggest that, when a small amount (2 cc.) of a virus of moderate potency is used, the thermal inactivation point is low, about 42.5 C. for thirty minutes. On the other hand, in one experiment the temperature necessary to produce inactivation was higher than 50 C. for thirty minutes, due probably to chance variation in the strength of the virus preparation. In other similar experiments, a temperature of 55 C. for all periods of from five to thirty minutes always produced inactivation of the virus.

This accords with the results of other investigators. When large amounts of a virus of moderate potency were used, the thermal inactivation was 52.5 C. for thirty minutes. Apparently an increase in the amount of virus injected caused the difference in the effect on monkeys. These results suggest that at temperature slightly above 40 C. (42.5 C.), the virus is possibly attenuated or, more probably, that part of the virus is destroyed so that a relatively small inoculum becomes ineffective in producing clinical poliomyelitis. Furthermore, as is shown in another paper, virus that is innocuous in a single injection may produce clinical symptoms of poliomyelitis on repeated injections.

AUTHORS' SUMMARY.

METABOLISM IN SCURVY; THE NITROGEN ABSORPTION AND RETENTION OF GUINEA-PIGS. H. L. SHIPP and S. S. ZILVA, Biochem. J. **22**:1449, 1928.

Young guinea-pigs were kept in metabolism cages and fed on a diet of bran, barley meal, middlings and fish meal, with daily doses of reconstituted dried milk; this diet, with 5 cc. of decitrated lemon juice daily, permitted of normal growth and health. In scorbutic animals the nitrogen balance and assimilation remained normal as long as the animal consumed its food; a negative balance was observed only when appetite failed in the prenatal phase.

KUGELMASS, New York.

HORMONES OF THE ANTERIOR PITUITARY LOBE. L. F. HEWITT, Biochem. J. **23**:718, 1929.

The anterior pituitary lobes of the ox were ground with sterile sand in a sterile mortar and extracted with tenth-normal sodium chloride or lime water in the cold over night. The mixture was neutralized to phenol red with tenth-normal hydrochloric acid or carbon dioxide, centrifugated and filtered through a Seitz filter. The filtrate kept for six weeks in the cold. Daily intraperitoneal injections into young adult female rats stimulated growth (12 Gm. per week instead of 3 Gm.), and a maximum weight of 300 Gm. instead of 180 Gm. was attained. Weight was lost immediately when the injections were omitted. It is suggested that they stimulated the thyroid, hyperactivity of which was responsible for the loss in weight. Throughout, estrual cycles occurred normally. Unfiltered alkaline extracts (to which sodium benzoate was added) contained the growth-promoting hormone, and sometimes inhibited estrums. The anterior pituitary lobes of the ox were extracted with tenth-normal hydrochloric acid and the extract treated with kaolin before centrifugalization; the supernatant fluid was neutralized, centrifugated and filtered; the filtrate contained no growth-promoting hormone, but one was present which produced premature sexual development when injected into immature rats, or follicular maturation when injected into adult rabbits. Hence the anterior lobe of the pituitary gland contains at least three hormones.

KUGELMASS, New York.

CULTIVATION OF VACCINIA VIRUS. H. B. MAITLAND and A. W. LAING, Brit. J. Exper. Path. **11**:119, 1930.

The technic and the results of experiments on the cultivation of vaccinia virus in mediums containing rabbit kidney or testis are presented. Little virus is necessary to initiate growth and in almost all cases there is an increase of from 10 to 1,000 times or more. The authors conclude, "In view of the regularity with which cultures have been obtained, the potency of culture-virus and the maintenance of its infectivity during storage, its freedom from bacterial contamination, and the small cost entailed, this or a similar method of culture suggests itself as being suitable for the production of 'vaccine' on a larger scale."

J. N. PATTERSON.

THE ANTI-DIURETIC EFFECT OF THE SEPARATED PRINCIPLES OF THE PITUITARY BODY. A. HEMINGWAY and J. M. PETERSON, J. Physiol. **68**:238 (Nov.) 1929.

The antidiuretic action of the oxytocic principle of the pituitary body and the pressor principle was demonstrated in experiments performed on a heart-lung-kidney preparation (Starling and Verney) and on water diuresis in man (produced by drinking 1 liter of water in fifteen minutes, and the subcutaneous injection of active principles); the concentration of urinary chlorides was increased in the isolated kidney preparation. Pitressin has a vasoconstrictor effect on the renal vessels. In man both extracts inhibit diuresis, but the pressor principle is twenty times more powerful than the oxytocic principle of the pituitary body. The antidiuretic action of the latter may be due to imperfect separation from the former.

KUGELMASS, New York.

CLINICAL STUDY OF THE PANCREAS. M. CHIRAY, A. JEANDEL and A. SALMON, Presse méd. **38**:977 (July 19) 1930.

A study of the enzymes of the pancreas was made by the intravenous injection of purified secretin. The dose was 16 mg. in 6 cc. of double distilled water which contained 144 mg. of lactose. Specimens were taken for examination at five minute intervals, by means of an Einhorn tube. As a preliminary measure, 33 per cent magnesium sulphate was given to empty the gallbladder; when A, B and C fractions had been taken, the injection was made. It was followed, almost immediately, by a tremendous increase in the volume and enzymatic content of the pancreatic secretion. The lipase curve showed the more marked initial rise.

In pancreatic insufficiency the response is delayed and the enzymatic curves vary greatly. The authors believe that their method has great value in cases in which the curve is normal, and in cases of cholecystitis before and after operation. They have not had enough cases to draw conclusions regarding other conditions.

BIEKER, St. Petersburg, Fla.

THE MENINGOCOCCI AND CEREBROSPINAL MENINGITIS. JUAN JOSÉ PIERAS ALEGRE, Med. de los niños **31**:104 (April) 1930.

The author discusses the possibility of there being a type of meningococcus that produces meningitis without attacking any other tissue, and a type that affects the joints or the blood, resulting in meningitis secondarily. The four types of meningococci and the effect of curative serums on infections caused by them are described.

DWYER, Kansas City, Mo.

THE MOTOR ACTIVITY OF THE SMALL INTESTINE: II. THE EFFECT OF INTESTINAL JUICE ON THE MOTOR FUNCTION OF THE SMALL INTESTINE. E. BABSKY and M. EIDINOWA, Arch. f. d. ges. Physiol. **222**:649, 1929.

The intravenous injection of intestinal juice obtained by means of a Thiry-Vella fistula in the upper part of the small intestine in dogs has little or no effect on the motor activity of the small intestine. The addition of from 0.5 to 1 per cent of lactic, hydrochloric or acetic acid to the intestinal juice markedly increases its effect, even after neutralization. The addition of gastric juice is less effective than that of acid. The injection of neutralized, acid-treated intestinal juice usually causes a rise in the tone and an increase in the contractions of the intestine. In 20 per cent of experiments there is a fall in tone and an inhibition of contractions. The activating effect of acid on the juice is not an enzyme action.

KUGELMASS, New York.

THE PHENOMENA ATTENDING FIRST DENTITION. F. GIERTHMÜHLEN, Arch. f. Kinderh. **90**:196 (May 24) 1930.

The author believes that the pendulum may have swung too far from the old idea that "teething" causes fever, gastritis and convulsions. He mentions two cases from his own practice in which a positive Chvostek sign and slight convulsions developed during teething. He believes that a latent tetany was aggravated by additional nervous strain.

SANFORD, Chicago.

EFFECTS OF IRRADIATED AND NONIRRADIATED ERGOSTEROL ON ARTERIES. W. HEUBNER, Beitr. z. path. Anat. u. z. allg. Path. **84**:559, 1930.

A number of investigators have described toxic effects caused by the administration of irradiated ergosterol in large doses to animals, especially rabbits. Among the effects produced is calcification in various organs and particularly in the arteries. It is also known that the feeding of cholesterol causes arterial changes. The question arises whether the effects brought about by irradiated ergosterol are in part effects of sterol, similar to those caused by cholesterol. In comparable feeding experiments, ergosterol, irradiated ergosterol and cholesterol were fed to rabbits of a strain that had previously been found susceptible to the action of irradiated ergosterol. The latter substance caused degenerative changes in the aorta with marked calcification of the lesions. Cholesterol, which was known to be free from ergosterol, caused atherosclerosis of the aorta without calcification. Nonirradiated ergosterol had no effect on the aorta. Some of the pathologic effects of irradiated ergosterol have been described as reversible, in that they disappear after the administration of the material is stopped. The arterial calcification caused by irradiated ergosterol was found by Heubner to be permanent.

SCHULTZ, Chicago.

DETECTION OF VITAMIN A. H. STEUDEL, Biochem. Ztschr. **207**:437, 1929.

The author claims to have isolated from fat a substance which, although it gives no blue color with antimony trichloride, contains sufficient vitamin A to maintain normal growth when administered to young rats.

KUGELMASS, New York.

THE ENDOCRINE FUNCTION OF THE PINEAL BODY. E. BRANDENBURG, Endokrinologie **4**:81 (July) 1929.

The author has studied a large number of pineal glands from human beings and pigs in order to test the hypothesis that there is a difference between the shape of the gland in men and in women, and that in women the number of pregnancies brings about definite variations in the organ. In histologic preparations variations in the calcium content and the amount of connective tissue have been sought. The conclusion is that both the round and the pointed glands are found in men and women of all ages. The calcium content is only regularly absent in childhood, and may be present in greater or less amount in later life. The connective tissue increases with age. There seem to be morphologic grounds for the assumption of an endocrine function of the pineal body.

KUGELMASS, New York.

STUDIES IN THE PHYSIOLOGY OF DIGESTION IN INFANTS: XI. HAS THE PROTEASE OF LEUKOCYTES AN INFLUENCE ON THE DIGESTION OF PROTEIN? O. BUDDE, Ztschr. f. Kinderh. **49**:116, 1930.

There is no evidence that the protease of leukocytes influences the digestion of protein. Repeated attempts to obtain a proteolytic ferment from lymphocytic tissue, the tonsils and the thymus of calves yielded no active preparation. The

study of the intestinal wall or of lymphatic tissue from the mesenteric glands would be useless because intestinal proteases occur in these tissues all the time.

EMERSON, Boston.

Nutrition

THE USE OF GELATIN AS A SUPPLEMENTARY FOOD IN THE INFANT'S DIETARY. THEODORE O. ELTERICH, D. H. BOYD and ANDREW NEFF, Arch. Pediat. **47**: 286 (May) 1930.

The article contains a historical summary and a detailed report of the progress of eleven infants fed on formulas containing gelatin.

The authors' summary is as follows: "1. Large amounts of gelatin may be administered to very small infants over fairly long periods of time without any apparent unfavorable consequences. 2. Contrary to previously reported studies, gelatin does not accelerate growth out of proportion to calories ingested. 3. Gelatin acts like protein matter, and gain in weight is in proportion to protein-carbohydrate ratio. 4. Our feeling would be that addition of gelatin to the formula produces results similar to those found when protein milk is added to formulae, but it must be remembered that gelatin is an incomplete protein. On the other hand, the addition of gelatin to a formula of an older infant is less likely to be distasteful than would be the case with high acid formulae. 5. One hundred calories of gelatin (four level tablespoonfuls of powdered gelatin) may be added to the day's formula without increasing the volume. This is an advantageous factor in cases where infants have a tendency to vomit, in cases where high cereal formulae are necessary, or in cases where it is difficult to get infants to ingest normal quantities of food. 6. Gelatin may be a food factor in certain unusual allergic infants, where the ingestion of either breast or cow's milk cannot be tolerated."

WADDELL, University, Va.

SOME DIFFICULTIES OF INFANT NUTRITION. E. A. BARTON, Practitioner **125**:36 (July) 1930.

In this short but well written paper, Barton first discusses the sugar factor in infant feeding. He points out the low percentage of sugar used by the American School in contrast to the high sugars used in England and on the Continent. He stresses the value of high sugar formulas for premature infants and postoperatively when infants fail to gain weight.

In a consideration of the vitamins, the author takes a conservative stand. He feels that the use of cod liver oil is superior to the use of irradiated milk or foods.

The questions of green stools, citration of milk and caloric feeding in infancy are also briefly presented.

SAPPINGTON, San Francisco.

CHRONIC DYSPEPSIA IN CHILDHOOD. ROBERT HUTCHISON, Practitioner **125**:42 (July) 1930.

In his introduction, Hutchison makes it clear that the term chronic dyspepsia, as applied to children, represents a condition of whose true nature pediatricians are still ignorant. The author divides the subject into three main divisions: (*a*) gastric, (*b*) hepatic and (*c*) intestinal. Under gastric dyspepsia, he classifies chronic gastritis and functional disorders of secretion and motility. Both of these conditions are, the author states, not at all common in childhood.

The hepatic form arises either from a deficiency of liver function or from a diet high in dairy products.

The intestinal type usually occurs in children over 6 years of age. It appears to result from a diet high in sugar and starch; "nervous overstrain," want of

fresh air and exercise, and the swallowing of infected mucus from an unhealthy throat may be factors.

The treatment consists in dietary regulation and adjustment of environment.

SAPPINGTON, San Francisco.

CONGENITAL ANOREXIA. G. F. STILL, Practitioner **125**:49 (July) 1930.

The author believes that in some cases anorexia may be on a congenital basis. The explanation of the mechanism involved assumes a hunger center in the brain. This center is stimulated by the blood stream when depletion of nutrient material reaches a certain point. At birth, the brain cells constituting the hunger center become sensitive to stimuli as the placental circulation is cut off and hence the available supply of nutrient material in the infant's blood becomes depleted. The author offers this possible explanation of the normal development of hunger in a new-born infant. In cases of so-called congenital anorexia there may be a failure of the brain to respond to the blood as it should when depleted of nutriment.

The author cites a few cases of congenital anorexia from his own experience.

SAPPINGTON, San Francisco.

HYPERTROPHIC STENOSIS OF THE PYLORUS AND OESOPHAGEAL OBSTRUCTION IN INFANCY. F. J. POYNTON, Practitioner **125**:54 (June) 1930.

From a series of 100 consecutive cases of pyloric stenosis over a six year period, the author brings out the main points in the condition: (1) In this series, the tumor was palpated in every case; (2) it was also demonstrated at operation by the surgeon; (3) the results of operation showed 80 recoveries and 20 deaths. The condition of the patients at operation was classed as follows: in 35 good, in 39 fair and in 26 poor and very poor.

Statistics from the series also showed that 84 of the infants were boys and 16 girls; 53 per cent were first-born children. Vomiting began in the first week in 19 per cent, in the second week in 23 per cent and in the third week in 22 per cent. Forty-five infants were entirely breast fed.

The author also discusses esophageal obstruction, which he differentiates from pyloric stenosis.

SAPPINGTON, San Francisco.

DWARFISM AND INFANTILISM. H. GARDINER-HILL, Practitioner **125**:97 (July) 1930.

In this well written and well illustrated paper, the author describes the common types of dwarfism and infantilism met with in medical practice which are amenable to medical treatment. Under dwarfism, he discusses (*a*) simple rickets, (*b*) renal rickets and (*c*) celiac rickets; he presents examples and photographs of each. He points out that delayed development may be of the so-called physiologic type, caused by prematurity or occurring in a patient with a family history of clearly delayed development. Under true infantilism, he classifies the following forms, with excellent descriptions of each: (1) idiopathic and (2) endocrine: (*a*) myxinfantilism, (*b*) pituitary infantilism and (*c*) eunuchoid infantilism.

The author's summary gives an excellent idea of the clearness of his paper.

SAPPINGTON, San Francisco.

A CASE OF CELIAC DISEASE. W. MIKULOWSKI, Arch. de méd. d. enf. **33**:416 (July) 1930.

The author reports a case of infantilism in a boy, aged 5, which he was able to follow for two and a half years. As is common in these invasions, the onset was insidious and the chronic course of the disease characteristic. The differential diagnosis included the elimination of such disorders as tuberculous peritonitis,

chronic colitis, Hirschsprung's disease, pithiatism (of Babinski) and leiasthenia (of Loeper). Treatment was sympatomatic and consisted in the administration of antifermentative products and the activation of protoplasmic functions along the lines laid down by Fanconi.

AMESSE, Denver.

VEGETABLE PROTEINS IN INFANT FEEDING. ALEURONE FROM THE SUNFLOWER. L. RIBADEAU-DUMAS, R. MATHIEU and L. WILLEMIN, Nourrisson **18**:161 (May) 1930.

The product remaining from sunflower seeds after the removal of cortex and fats is rich in vegetable proteins and phosphates. It is also rich in calcium and magnesium, but lacks sodium chloride. Experiments on white rats show this product (aleurone) to be poor in vitamin A but rich in vitamin B. The proteins are inadequate for growth, but can be made adequate by the addition of lactalbumin or brewers' yeast.

Clinical trials have led the authors to adopt a formula containing: rice flour 10 Gm., sugar 5 Gm., malt 2.5 Gm., litmus 4 Gm. and water 76.5 Gm. This mixture contains 700 calories per liter. Infants fed on the mixture will gain for a period of three weeks and then the weight will remain stationary. The further addition of brewers' yeast to the mixture seems to supply the deficiency and enable an infant to thrive for an indefinite period.

The indications for the use of litmus will be given in a later communication.

MCCLELLAND, Cleveland.

THE DIETETIC TREATMENT IN DIGESTIVE DISTURBANCES OF INFANCY. L. MOLL, Rev. franç. de pédiat. **6**:177, 1930.

Protein is again implicated by Professor Moll as a cause of nutritional disturbances in infancy. He cites the work of Schiff, who with his collaborators has shown that the toxic syndrome is produced not by the restriction of water alone but only by the restriction of water and the administration of protein. Since 1922, except in cases of diarrhea accompanied by very acid stools, in which albumin milk is used, Moll has used as therapeutic foods mixtures that are poor in protein. The principal element in these is a filtrate from milk in which the protein has been precipitated by boiling with calcium lactate. To this he adds either breast milk, almond milk or a cereal pudding. By the use of such preparations, he feels that he is able to shorten the period of starvation and fulfil the caloric requirements of the infant at a much earlier date than when other preparations are used. Since the regimen has been instituted, the mortality figures in cases of severe diarrhea have fallen from 32 to 5.1 per cent. Even for healthy infants, he advocates the minimum amount of protein in the diet.

LESLIE, Evanston, Ill.

RICKETS AMONG CHILDREN INFECTED WITH MALARIA. GIOVANNI CAREDDU, Clin. pediat. **12**:243 (March) 1930.

This paper represents an extended study of rickets, from the statistical and clinical standpoint, in children infected with malaria in the province of Cagliari. Careddu arrives at the following conclusions: 1. In the province of Cagliari rickets among children under 2 years of age is rare (9 per cent.). 2. In children infected with malaria after the second year of life rickets occurs in a higher percentage of infants (50 per cent). 3. Rickets may be seen in early life, even during the first six months, if malarial infection has occurred at this age. 4. In these early cases the clinical manifestations of rickets are referred particularly to the bones of the skull and face. An enlarged head, a saddle-back nose and the characteristic facies of congenital syphilis are seen with such regularity that in regions where malaria is prevalent these observations lose their importance in the diagnosis of syphilis. 5. These clinical observations are always associated with

a low phosphate index, and often with anemia and splenomegaly. 6. The treatment must be primarily antimalarial, and secondarily antirachitic.

SIGNORELLI, New Orleans.

A CASE OF DYSTROPHY ALIPOGENETICA (BLOCH). M. DA ROCHA, JR., Arch. de pediat., Rio de Janeiro **2**:688 (July) 1930.

Da Rocha reports a case of dystrophy alipogenetica in a boy, aged 19 months and weighing 5,100 Gm., who had been fed exclusively on farina. He was extremely emaciated and pale, and had keratomalacia. Recovery was prompt after a proper diet containing vitamins A and D was instituted.

SANFORD, Chicago.

THE CRUSADE AGAINST RICKETS. E. NASSAU, Arch. f. Kinderh. **90**:26 (March 28) 1930.

The author gives the results obtained in the treatment for rickets at a day sanatorium in a quarter of Berlin inhabited by poor people. This institution has been operated for two years and has been of great value, both in prophylaxis and in stopping active processes. The muscle tone, static deformities and skeletal deformities are all greatly improved. The low cost of operating such a sanatorium makes it of further value. The children are brought to the institution early in the morning and are given a bath. At 8 a. m., they have breakfast, after which three hours are devoted to gymnastics, irradiation, play and kindergarten. At 12 o'clock they have dinner and spend two hours lying in the open air. At 3 p. m. lunch is served and then two hours are spent in play and in kindergarten. At 5:30 p. m. the children have supper and at 6 o'clock they are called for by their parents.

SANFORD, Chicago.

IRRADIATED MILK IN THE TREATMENT FOR RICKETS. O. ANDRESEN, Arch. f. Kinderh. **90**:65 (March 28) 1930.

Andresen describes the three types of irradiation of milk used in the Children's Hospital at Kiel, and he gives sketches of the apparatus (Hannauer, Wamoscher and Buhtz). In a series of forty children, all were relieved of rachitic symptoms after the use of irradiated milk. Phosphorus and calcium determinations were made during the trial period. The results showed little difference between the different methods of irradiation of milk; in all instances a uniform rise occurred.

SANFORD, Chicago.

THE MODIFICATION OF THE METABOLISM OF NORMAL CHILDREN BY MEANS OF SALT MIXTURES. F. BOLDT and M. WINTER, Arch. f. Kinderh. **90**:83 (March 28) 1930.

The authors studied two normal children on a controlled diet plus 5 Gm. of salt mixtures. The blood calcium, phosphorus, sodium chloride and alkali reserve was checked and the urine titrated for acidity. The principal changes were in the ammonia of the urine and in the nitrogen balance. In the first child the normal readings were 106.45 mg. and 0.163 mg., respectively. After the administration of salt mixtures for two weeks the ammonia was reduced to 72.9 mg. and the nitrogen balance had risen to 2.313 mg. In the second child the ammonia and nitrogen balance were changed from 152.47 mg. and 0.633 mg. to 92.748 mg. and 2.80 mg., respectively.

SANFORD, Chicago.

FUNCTIONAL DISTURBANCES OF THE DIGESTIVE TRACT IN INFANTILE BERIBERI. K. OHTA and T. IZUMITA, Jahrb. f. Kinderh. **128**:10 (June) 1930.

The form and the peristaltic movement of the stomach in infantile beriberi are normal. The emptying of the stomach is delayed; whereas human milk leaves the

stomach of the normal infant sooner than does cow's milk, the milk of women suffering from beriberi is retained longer than cow's milk both by normal infants and by those with beriberi. This is not due to an absence of vitamin B in the milk or to alterations in the kind or amount of fat. Controlled studies with moderate doses of pilocarpine, atropine and epinephrine failed to explain the motor disturbance.

CLAUSEN, Rochester, N. Y.

ACTION OF VIOSTEROL ON ARTERIES. W. HEUBNER, Klin. Wchnschr. **8**:407 (Feb. 26) 1929.

Rabbits were given 40 mg. of viosterol daily. They all died in from nine to ten and one-half days, and showed marked sclerotic changes in the aorta and its branches. In the renal arteries, degenerative changes were found also in the middle coat. The antirachitic action of viosterol was relatively weak. The author reviews the experiments of others on the toxicity of preparations of irradiated ergosterol, and concludes that at present they show no differences in the ratio of the toxic to the therapeutic dose. He suggests that the toxic and therapeutic principles are identical.

KUGELMASS, New York.

THE TOXIC EFFECT OF COD LIVER OIL. E. AGDUHR, Monatschr. f. Kinderh. **47**:97, 1930.

In studies begun in 1919 and 1920 on the subject of postfetal development and increase of nerve fibers, Agduhr used a variety of diets with the addition of cod liver oil. The experimental animals were white rats, rabbits, dogs, cats and calves. The dosage of cod liver oil varied from 0.14 cc. per kilogram daily to 5 cc. The animals receiving the large dose gained less in weight than those on the smaller doses; indeed, the larger dose seemed definitely harmful. Pregnant animals that were given this dosage often died. Calves seemed susceptible to a dosage of 1.6 cc. per kilogram daily.

The injuries apparently produced by the oil were: functional cardiac changes, changes in the cardiac conduction system as shown by the electrocardiogram, microscopic degenerations in the heart muscle and the liver, fatty infiltration in the walls of the entire gastro-intestinal tract, gastric ulcer, degenerative fat infiltration, hemorrhages and necroses in the liver, degenerative changes in the kidneys and adrenals and sclerotic and degenerative changes in practically all the organs of the body, even the bones.

The blood showed anemia with an increase of white cells, especially of polymorphonuclears. The author has attempted to isolate the harmful factor in the oil, but so far he has been unsuccessful.

GERSTLEY, Chicago.

Prenatal Conditions

HEREDITARY DEFORMING CHONDRODYSPLASIA, OR MULTIPLE EXOSTOSES. K. HALE, Ann. Surg. **91**:92 (July) 1930.

The author reports three cases of hereditary deforming chondrodysplasia. A father and two daughters showed similar multiple symmetrical exostoses. Fifty other cases have been collected from the English literature since 1917.

The etiology is a disorder of growth. There may be no symptoms unless there is a partial loss of joint function from a large exostosis, or pain from a pointed exostosis. The diagnosis is made by roentgenologic examination. If treatment is necessary, maturity is the time indicated for corrective operations.

SANFORD, Chicago.

CONGENITAL DEFORMITIES OF THE EXTERNAL EAR: THEIR MENTAL EFFECT. C. R. STRAATSMA, Arch. Otolaryng. **11**:609 (May) 1930.

Photographs are shown of patients with various deformities of the external ear, both before and after operation. These include microtia, deformities due to

intra-uterine pressure, protrusion and partial loss of the helix and large protruding ears. A plea is made for early correction of these abnormalities because of the injurious effect that they have on the mental attitude of the child.

BARNETT, Chicago.

CONGENITAL ATRESIA OF THE TRICUSPID ORIFICE. PAUL J. BRESLICH, Arch. Path. **10**:206 (Aug.) 1930.

In addition to congenital atresia of the tricuspid orifice an infant had associated defects of the inter-auricular septum, hypoplasia of the right ventricle and a subaortic defect of the interventricular septum. Clinically the infant showed marked cyanosis, and there was a loud systolic murmur over the mitral precordium. The embryology of the condition is discussed.

LESLIE, Evanston, Ill.

CONGENITAL CYSTIC LUNG. IRVING J. WOLMAN, Bull. Ayer Clin. Lab. Pennsylvania Hosp., 1930, no. 12, p. 49.

A case of congenital cystic lung in a six months stillborn fetus, discovered in the course of a routine necropsy, is recorded. The author holds that the cystically dilated intercommunicating bronchioles and alveoli form a closed system, or systems of chambers, not continuous with the main bronchi.

KOBAK, Chicago.

PERSISTENCE OF VITELLO-INTESTINAL TRACT IN AN INFANT. SIDNEY BOYD, Proc. Roy. Soc. Med. **23**:993 (May) 1930.

An infant, aged 14 days, was admitted to the hospital with a large umbilical stump about 1 inch (2.5 cm.) long, the apex of which was covered with granulations. There was an intermittent discharge of fecal matter from a minute orifice at the apex.

WILLIAMSON, New Orleans.

CONGENITAL SCOLIOSIS IN A CHILD; SIMILAR MALFORMATION IN THE MOTHER. R. DUCROQUET and C. MAROT, Bull. Soc. de pédiat. de Paris **27**:385 (July) 1929.

A child showed congenital scoliosis which roentgenologic examination revealed to be due to the interposition of two hemivertebrae, one on the right side between the second and third lumbar vertebrae and the other between the eighth and ninth dorsal vertebrae on the left side, the latter having a rib attached to it. There were twelve ribs on the right side and eleven ribs on the left side. Roentgenologic examination of the mother's spine showed scoliosis due to a hemivertebra between the twelfth dorsal and first lumbar vertebrae with a rib attached to it; the third lumbar and the fourth dorsal vertebrae were formed of two hemivertebrae in juxtaposition; the fourth and fifth lumbar vertebrae had hypertrophied transverse processes on the right side which were joined together.

BENJAMIN, Montreal, Canada.

TWO CASES OF CONGENITAL ABSENCE OF BOTH RADII. M. MARQUEZY, DUCROQUET and LEMASSON, Bull. Soc. de pédiat. de Paris **27**:388 (July) 1929.

In a girl, aged 3 years, the forearms were atrophied and shorter than normal and the hands were turned toward the outer aspect of the forearms; there was atrophy of the thenar eminence and of the thumb and deviation of the phalanges of the lateral three fingers toward the inner border of the hand; there was some atrophy of the shoulder muscles. The child grasped objects between the index and the outer three fingers, but could not oppose the thumb on to these fingers. The hand could not be straightened out, but the deformity could be exaggerated

so that the thumb touched the forearm. The lower extremities showed genu varum, more marked on the left, and the tibia of each leg was internally rotated on the femur.

A boy, aged 15 months, showed complete absence of the radius and thumb of each upper extremity, and also spina bifida occulta from the sixth cervical to the tenth dorsal vertebrae. He also showed a rare condition, viz., articulation between the petrous temporal bone and the bones of the cranium.

BENJAMIN, Montreal, Canada.

CONGENITAL PARTIAL HYPERTROPHY. L. MAGNI, Riv. di clin. pediat. **28**:688 (Aug.) 1930.

Magni reports a case of congenital partial hypertrophy in a girl aged 5½ years. From birth, the right side of the body was observed to be larger than the left. Hypertrophy was observed in the eye, nares, tongue, arm and leg on the right side.

HIGGINS, Boston.

DOLICHOSTENOMELIA OF A FAMILIAL CHARACTER, SHOWING SUPERNUMERARY ZONES OF OSSIFICATION. G. FRONTALI, Scritti medici dedicati a Carlo Comba, ediz., Riv. di clin. pediat., 1929, p. 108.

A man, his daughter and two sons, aged 7¾ and 14 years, had dolichostenomelia (i. e., long narrow extremities); the mother and three other children were normal.

The author studied the two boys carefully; he gives anthropometric data, roentgenograms and photographs, as well as the results of physical examination, tests of electrical excitability of the muscles, tests of basal metabolism and the nitrogen and fat metabolism, the blood chemistry and functional tests of the vegetative nervous system. Aside from the skeletal changes, the boys were normal.

The phalanges of the hands, the first metacarpals, the phalanges of the big toes and the first metatarsals showed two epiphyses; this anomaly permits of growth in both directions. The author has not found mention of this condition in the description of other cases in the literature.

HIGGINS, Boston.

EXUDATIVE DIATHESIS. RAUL FERNANDEZ CORDOBA, Arch. am. de med. **6**:91 (July) 1930.

The author discusses the diagnosis and treatment in a case of scrofula urticarius in an infant aged 1 month. A dietetic regimen particularly low in fat is important. The injection of whole blood is often of particular and striking benefit. It is given intramuscularly and in a dosage beginning with 3 cm. and increasing to 9 cm.

SCHLUTZ, Chicago.

CONGENITAL HYDRONEPHROSIS. A. JOHOW and R. GANTES, Arch. de hosp. de niños Roberto **1**:128 (June) 1930.

The authors report a case of congenital hydronephrosis in a child, aged 1 month. At operation a large kidney was found on the right side, with an enormously dilated pelvis. There was abnormal implantation of the ureter, causing almost complete obstruction. The infant recovered from the operation and had no difficulty with the urinary excretion, but died in about a week from an unrelieved intestinal obstruction caused by adhesions.

SCHLUTZ, Chicago.

ANENCEPHALY AND HYPOPLASIA OF THE SUPRARENAL GLANDS. G. B. GRUBER, Beitr. z. path. Anat. u. z. allg. Path. **84**:335, 1930.

The frequent association of anencephaly with hypoplasia of the suprarenal glands led Gruber to make a study of the topography of these glands in a series

of anencephalic monsters. The suprarenal glands were found to be hypoplastic in twenty-five of twenty-six examples of anencephaly studied. In the twenty-sixth case the suprarenal glands could not be found. In a case of hemicrania with cerebral hernia, the suprarenal glands were abnormally small. In two examples of occipitocervical craniorhachischisis, the suprarenal glands were of normal size. Hypoplasia of these glands, was frequently associated with malposition; the left often lay behind the vena cava, and the right had a position more ventral to the kidney than normal. In five of the anencephalic monsters, the cranial and vertebral deformities were associated with ventral abdominal hernia. Abnormality in the size and shape of the abdominal cavity due to the deformity caused by defective vertebral closure is probably a factor in this relatively high incidence of ventral hernia in anencephaly. In the five examples of ventral hernia, the kidneys had a position higher than normal, the upper pole being situated high up under the diaphragm. In each instance the diaphragm was closed, an observation that is not in accord with the theory of Kleine that high position of the kidneys may be a cause of diaphragmatic hernia.

SCHULTZ, Chicago.

CONGENITAL ABSENCE OF OVARIES WITH INFANTILISM. R. RÖSSLE and J. WALLART, Beitr. z. path. Anat. u. z. allg. Path. 84:401, 1930.

Rössle and Wallart precede the detailed presentation of a case of congenital absence of the ovaries with infantilism by a discussion of the criteria that must be met before absence of the ovaries may be accepted as congenital, originating in fetal life. Following Morgagni's first careful description of the condition, many reports appeared in the earlier literature. These cases cannot be accepted because the absence of ovarian tissue was not verified microscopically. With the development of histology, the subject disappeared from the literature. Only during the past decade have there again appeared reports of congenital absence of the ovaries verified by careful microscopic examination. The authors accept as valid only the cases of Olivet, Robert Meyer and Randerath, reported in 1925, the case of Schürmann reported in 1927 and their own case. They also accept Morgagni's case because of the classic completeness of his description. They leave out of consideration clinical cases of infantilism supposedly due to absence of the ovaries. Their patient was a woman, aged 30, whose death was due to a gliosarcoma of the cerebellum. She had ceased to grow at 8 or 9 years of age. Mentally, she had been normal. At necropsy, the body was 133.5 cm. long. The size of the body and the proportions of the body and of the internal organs were those of a girl before puberty. The breasts were not developed, and axillary and pubic hair was absent. The internal labia were absent, but otherwise the internal and external genitalia were like those of a girl 11 years of age, except that the ovaries were absent. Careful microscopic examination of the adnexa, uterus and vagina failed to reveal any ovarian tissue. The rete ovarii was present. This contained well differentiated tubules and others that resembled the tubules of the primitive kidney. With the latter were tubular structures that had the morphology of ducts of the epididymis and others similar to the hydatid of Morgagni. At one point, tubules of primitive renal origin formed an adenomatous nodule, and two areas of misplaced cortical suprarenal tissue were encountered. The authors conclude that theirs is an example of true congenital absence of the ovaries, and that the infantilism was due to this defect. The embryonic period at which the defective development first manifested itself or its cause could not be determined. They consider a disappearance of the primitive sex cells in early fetal life most probable. The fact that the rest of the genital system was normally developed indicates that the development of the rest is not dependent on the ovary; these sexual characters are predetermined in the zygote. The rete ovarii and the rete testis are derivatives of the primitive kidney.

SCHULTZ, Chicago.

THE ENDOCRINE FUNCTIONS IN FETAL LIFE. E. J. KRAUS, Endokrinologie **5**:133 (Oct.) 1929.

From an examination of the evidence of other workers, and especially from the study of a case of total absence of thyroid and changes in other glands in a new-born child, the author concludes that the endocrine glands are active in fetal life, at any rate, to a partial degree.

KUGELMASS, New York.

Acute Infections

NOTE ON THE DIAGNOSIS OF PNEUMOCOCCUS PERITONITIS FROM THE BLOOD PICTURE. CHARLES L. GIBSON, Am. J. M. Sc. **180**:344 (Sept.) 1930.

Graphic illustrations are presented to contrast nonpneumococcic and pneumococcic types of peritonitis with reference to the leukocyte-polymorphonuclear ratio.

Severe forms of ordinary peritonitis have a relatively low leukocytosis and a fairly high polymorphonuclear percentage.

Pneumococcus peritonitis has an extraordinarily high leukocytosis and a high polymorphonuclear percentage.

Secondary forms are observed only in males and both primary and secondary forms in females; in the latter instance they occur mostly in girls from 4 to 7 years of age. The portal of entry is through the genital tract.

Pneumococcus peritonitis, while uncommon, is not rare, and this blood picture may aid in the differential diagnosis.

HENSKE, Omaha.

THE PROGNOSIS FOR EPIDEMIC ENCEPHALITIS IN CHILDREN H. A. HOWE, Bull. Johns Hopkins Hosp. **47**:123 (Sept.) 1930.

Of 115 patients who were recorded as having had epidemic encephalitis, only 66 were selected for study because of difficulty in confirming the diagnosis or in following the cases; 70 per cent were reached at least 6 years after their initial illness, and 47 per cent after an interval of more than 8 years. The difficulty of determining intellectual damage at an early age is appreciated, as is the importance of prolonged observation.

The initial acute illness is grouped under three headings: (1) the somatic form (56 per cent of the cases), characterized by paralysis or excitation of the somatic or cranial nerves; (2) the meningeal form (16 per cent), in which signs of meningeal irritation predominate and there is a relatively high cell count in the cerebrospinal fluid, and (3) the abortive form (19 per cent), in which the acute condition begins with phenomena usually considered as sequelae (excitement, bizarre activity, sleeplessness).

The author gives the following summary:

1. The immediate mortality, based on all hospital admissions since 1918, was 11 per cent.

2. It was further shown that the immediate mortality was higher in the somatic group and at early ages, that recovery was almost invariable in the meningitic form, and that the most dreaded sequel, parkinsonism, ensued most frequently after the abortive form.

3. Complete incapacity was found in 19 per cent, partial incapacity in 22 per cent and recovery in 42 per cent.

4. Sequelae were divided into progressive and nonprogressive, the former including hyperactivity (usually of a bizarre type), sleep inversion, personality changes, hyperpnea, tics, etc. (all excitation phenomena), the latter characterized by residua of the acute illness in the form of paralyses, choreiform movements, emotional instability and mental retardation.

5. The nonprogressive sequelae most frequently followed the general somatic type of acute illness and, with the exception of mental retardation, offered a good prognosis.

6. The progressive sequelae justified an unfavorable outlook, and, when present as initial symptoms concomitant with the acute illness, almost invariably led to parkinsonism.

7. Parkinsonism was further shown, as far as this series was concerned, to ensue only after a characteristic type of progressive (excitation) sequelae.

LYTTLE, New York.

CONVALESCENT MEASLES SERUM AS A SPECIFIC THERAPEUTIC MEASURE. HARRY A. SAVITZ, M. J. & Rec. **132**:114 (Aug. 6) 1930.

The author gives a brief summary of what has been found about the etiology of measles and of what has been done in using immune serum in the prevention of the disease and in the treatment for it. He then gives a report of a case in which he used the serum of a convalescent patient in the treatment of a patient with measles. He thinks that his results were good.

WILLIAMSON, New Orleans.

SEPSIS IN INFANCY AND CHILDHOOD. I. ABT, Nebraska M. J. **15**:297 (Aug.) 1930.

Sepsis is a general infection of the entire organism without a definite or specific visceral change. The cause of general sepsis is explained not by the multiplication of micro-organisms in the blood, but by their constant or periodic entrance into the blood stream from a focus of infection. The virulence of an organism is a fluctuating and relative quantity and varies in the relation to the response of the defense reactions of the body. The latest view is that a major portion of the defense reactions depends on the efficiency of the reticulo-endothelial system, that is, according to Aschoff, the reticulum cells of the splenic pulp, the malpighian corpuscles, the bone-marrow, the lymph nodes and other lymphatic tissues. If the phagocytes of the reticulo-endothelial system fail to take up the bacteria, the latter continue to swarm in the blood stream, and an overwhelming form of sepsis occurs. The author doubts that successful resistance to bacterial infection depends on the response of the endocrine glands. All infants, especially the premature and artificially fed, are particularly susceptible to septic infection. In infancy sepsis is characterized by a sudden onset and a severe course. The demonstration of a primary focus is not always possible. During childhood, the tonsils are the most frequent atrium for septic infection. Every case of tonsillar infection or angina offers a possibility. One is struck by the variety and multiplicity of manifestations. The history of chills is of the greatest importance. A chill signifies that the focus of infection is in communication with the blood stream, and that the bacteria have gained access to the circulation. The local symptoms may improve, but the chills, fever and metastases continue. As a rule, there is a marked contrast between the mild local symptoms and the severe general condition. Cases of postanginal sepsis offer an unfavorable prognosis, as a rule. The acute type develops rapidly, and may cause death in two or three days. The chronic form manifests itself as rheumatism or recurrent endocarditis. A third form is characterized by agranulocytosis, which first involves the tonsil and has a characteristic blood picture. The agranulocytosis is probably not a distinct disease, and it should be regarded as a reaction of the organism to a septic infection. No satisfactory method of treatment is known. The early eradication of the focus of infection is the most satisfactory. No satisfactory chemotherapeutic agent for the treatment in sepsis has been found. Drugs, dyes and serums have largely been disappointing. Opinion is divided as to the benefits of the injection of blood.

HAMILTON, Omaha.

PREVALENCE AND TREND OF MENINGOCOCCUS MENINGITIS IN THE UNITED STATES. R. C. WILLIAMS, Pub. Health Rep. **45**:1657 (July 18) 1930.

Attention is called to the increase of meningitis in the United States. In 1925, there were 1,859 cases; in 1926, 2,226; in 1927, 3,204; in 1928, 5,781, and in 1929,

9,660. The important measures to be considered are: (1) prompt recognition of cases of the disease, (2) a prompt report to the health authorities, (3) the avoidance of overcrowding, (4) the maintenance of high standards of bodily vigor, (5) sterilization of dishes and eating utensils and (6) the optimum amount of fresh air and sunshine for carriers and convalescents.

SANFORD, Chicago.

THE PRESENT STATUS OF STREPTOCOCCUS BIOLOGIC PRODUCTS IN THE PREVENTION AND TREATMENT OF SCARLET FEVER. M. V. VELDEE, Pub. Health Rep. **45**:1827 (Aug. 8) 1930.

There are certain shortcomings in streptococcic biologic products that need correction before the health officer can afford to push their use energetically. This in particular refers to the practice of giving five injections of toxin, low in potency and relatively high in protein content, which causes annoying reactions in a fairly large percentage of those treated. Until this defect is corrected, the use of these products by the practicing physician will remain limited, and the public will not accept them to any great extent.

SANFORD, Chicago.

PARENTAL BLOOD SERUM IN THE PROPHYLAXIS AND TREATMENT OF MEASLES. F. LEE BIVINGS and ROGER W. DICKSON, South. M. J. **23**:880 (Oct.) 1930.

Of 103 children treated by the injection of parental blood serum, 71 were given complete protection and 32 had measles in a modified form. The authors gave the serum of convalescent persons. The blood was taken from the parent or another suitable donor, provided he had had measles at some previous time.

The authors believe that for complete protection a minimum of 0.5 cc. of serum per pound of body weight must be given on or before the fourth day after exposure. If more time has elapsed the dosage must be increased.

The method is free from danger. No untoward reactions were observed.

SCHLUTZ, Chicago.

GANGRENE ASSOCIATED WITH SCARLET FEVER. S. SUTHERLAND, Brit. J. Child. Dis. **27**:102 (April-June) 1930.

In a Hebrew boy, 4½ years of age, following a mild attack of scarlet fever gangrene of the left leg developed. The condition was first noted on the eighteenth day of illness. Amputation was performed at the end of the sixth week. The amputated leg was carefully dissected, and no evidence of thrombosis or embolism was found. The child made a satisfactory recovery.

Another instance of gangrene following scarlet fever, also from the author's practice, occurred in a boy, aged 4 years, who was noticed to have dark purple patches on the arms and later on the trunk and feet, following acute nephritis and otitis. The patient died on the forty-second day of illness; no autopsy was obtained.

LANGMANN, New York.

SCARLET FEVER. J. BAHOV, Arch. de méd. d. enf. **33**:327 (June) 1930.

Basing his observations on more than 1,000 cases in the isolation hospital at Jassy, Bahov has found it convenient to classify his patients into 11 groups, according to the intensity of the infection and the degree of resistance offered, which he describes with considerable detail. The serum of convalescent patients is used exclusively in prophylaxis and treatment, much larger doses being employed than in America. The author contrasts its use with that of specific serums and finds the latter much less effective.

AMESSE, Denver.

CHANGES IN THE SPINAL FLUID IN ENCEPHALITIS FOLLOWING MUMPS. R. J. WEISSENBACH, G. BASCH and M. BASCH, Paris méd. **1**:531 (June 7) 1930.

The spinal fluid is clear, without coagulum and under increased pressure. In only a few cases was the albumin increased. The sugar was either normal, or slightly increased or decreased. The chlorides were normal. The cellular elements were about 50 per cubic centimeter, and the majority were lymphocytes. No organisms were found. The Wassermann reaction and colloidal gold curve were negative and the Pandy and Nonne-Appelt reactions variable.

SANFORD, Chicago.

DIPHTHERIA IN INFANCY. P. LEREBOULLET, Progrès méd., June 14, 1930, p. 1045.

In the infant diphtheria exists in five forms, the commonest being the nasal type. This is characterized by a chronic coryza and conjunctivitis. The second type is an intoxication. The third type frequently does not disclose the organism that is usually found in the nose; in this the child has symptoms resembling athrepsia. The fourth is the chronic nasal type in which there is possibly only an occasional chronic coryza; these children are carriers. The last type is that of cord infection caused by the bacilli.

SANFORD, Chicago.

MENINGITIS DUE TO BACILLUS COLI. A. BARDISIAN, Pediatria **38**:777 (July 15) 1930.

The author reports four cases of purulent meningitis due to infection with *Bacillus coli*, which showed the typical manifestations of this disease. Three of the patients were of suckling age and one was a boy aged 7 years.

The bacteriologic diagnosis was proved in each by both morphologic and cultural tests, and in two of the cases also by agglutination tests.

SIGNORELLI, New Orleans.

THE AMOUNT OF CALCIUM AND POTASSIUM IN THE BLOOD SERUM IN DIPHTHERITIC INFECTIONS. F. PEOLA and E. INGLESSI, Riv. di clin. pediat. **28**:745 (Sept.) 1930.

The blood of forty-eight patients with various stages and degrees of diphtheria was analyzed for potassium and calcium. In the milder cases, the calcium may be slightly lower than normal (from 9 to 10.5 mg. per hundred cubic centimeters), but the potassium and the potassium : calcium ratio is essentially unchanged. In the more severe cases showing toxemia and paralysis, the calcium is markedly lowered (between 7.1 and 9.9 mg. per hundred cubic centimeters) and the potassium : calcium ratio increased.

The authors found that the hyperexcitability of the muscles was not accompanied by a definite change in the potassium : calcium ratio; therefore they conclude that the neuromuscular hyperexcitability of diphtheria cannot be wholly explained by the action of the potassium and calcium ions, but that it must also be influenced by degenerative alteration of the muscle fibers and nerve endings.

HIGGINS, Boston.

POSTVACCINAL NERVOUS SYNDROMES. C. MALOSSI, Riv. di clin. pediat. **28**:776 (Sept.) 1930.

The author divides the diseases of the nervous system following vaccination for smallpox into two groups: (1) true vaccinal encephalomyelopathy, in which the virus becomes located in the central nervous system, and (2) the flare-up of a latent infection due to a temporary loss of resistance.

HIGGINS, Boston.

THE MORBIDITY OF DIPHTHERIA AND THE REACTION OF SCHICK. E. MERLINI, Riv. di clin. pediat. **28**:789 (Sept.) 1930.

The author presents some statistics obtained on the Schick test in the Provincial Infant Asylum at Genoa.

He compared the Schick reactions of mothers and their infants under 8 months of age. In ten cases in which the mothers and their infants, both giving positive Schick tests, the mother's reaction showed the larger erythematous zone. Of thirty-four cases in which the infants were 4 months of age or less, the reactions of the mother and her child were the same in thirty-three (twenty-seven being negative and six positive); in one case, the infant's reaction to the Schick test was negative and that of the mother was positive. Of thirty-one cases, in which the infants were between 5 and 8 months of age, the reaction of the mother and her child were the same in fifteen (eleven negative and four positive) and different in sixteen; in each of these sixteen instances, the infants' Schick reaction was positive and that of its mother negative.

Merlini observed 100 children between 1 and 6 years as to their reaction to the Schick test and as to the morbidity of diphtheria. They were divided into 6 groups as follows: (1) positive reaction, not carriers of germs, 65 patients; (2) positive reaction, carriers but without clinical diphtheria, 8; (3) positive reaction, clinical diphtheria, 7; (4) negative reaction, carriers but without clinical diphtheria, 2; (5) negative reaction, clinical diphtheria, 2, and (6) negative reaction, not carriers of germs, 16.

HIGGINS, Boston.

PREVENTION OF DIPHTHERIA BY TOXIN-ANTITOXIN, ITS ORGANIZATION AND RESULTS OBTAINED. R. TAVARES, Arch. de hyg. **4**:113, 1930.

The author's method of handling an epidemic of diphtheria is as follows: When a case occurs, all children below 11 years of age in the family and in the vicinity should be immunized with the toxin-antitoxin mixture without a Schick test. Persons over 11 years of age, especially in the case of contacts, should be given the Schick test and immunized if susceptible. From August to December, 1928, the Bureau of Infectious Diseases in Sao Paulo gave 3,297 immunizing doses of toxin-antitoxin to contacts and neighbors. No failure has been registered. The author thinks that active immunization should be made compulsory in localities where the disease is endemic.

SANFORD, Chicago.

THE SYNDROME OF ICTERUS GRAVIS IN TYPHOID FEVER. JOSE BONABA and R. CHARLONE, Arch. pediat. del Uruguay **1**:322 (June) 1930.

The authors report a case of typhoid fever in a boy, aged 3 years, who presented this symptom and who died on the ninth day. The process was extremely toxic from the beginning, and ran a fulminating course.

At autopsy a large inflammatory mass was found in the hilus of the liver, compressing and partly obliterating the biliary passages.

SCHLUTZ, Chicago.

INFECTIONS OF THE THROAT RESEMBLING DIPHTHERIA. HILDE GLASER, Monatschr. f. Kinderh. **47**:169, 1930.

The author reports one case of influenza and two cases of pneumococcus infection of the throat with a membrane that clinically looked diphtheritic but that was proved not to be on bacteriologic examination.

GERSTLEY, Chicago.

THE LUNG IN PERTUSSIS. O. GÖTTCHE and G. ERÖS, Monatschr. f. Kinderh. **47**:204, 1930.

Pertussis causes a chronic inflammation of the lung tissue the origin of which is in the hilar glands. There is a simultaneous bronchial catarrh with perivascular

and peribronchial inflammation extending along the lymphatics to form areas of inflammation in the interstitial tissue. This period, which takes about a month, is characterized by a slight temperature and cough, with indefinite auscultatory symptoms. A lung affected by pertussis virus is particularly susceptible to mixed infection. Even with a mixed infection, the typical process of pertussis, with its greatest activity in the hilar region, can be distinguished.

The enlargement of the hilar glands tends to obscure the cardiac outline. In 40 per cent of their cases, Göttche and Erös describe a triangular shadow, composed of the heart and glands, which they consider typical of pertussis.

GERSTLEY, Chicago.

AN EPIDEMIC OF PFEIFFER'S GLANDULAR FEVER. K. SCHEER, Monatschr. f. Kinderh. **48**:59, 1930.

The author reviews the literature on Pfeiffer's disease and reports an epidemic of the condition, which he considers a definite entity; forty-three children and two nurses were affected.

In the majority the onset was sudden with a rapid rise of temperature to 40 C. (104 F.). After two days the temperature fell and the swelling of the cervical lymph nodes increased. This was usually bilateral. Five cases were severe; in two of them abscesses developed.

The appearance of the throat is characteristic. There is not so much marked erythema and inflammation of the tonsils and uvula as there is a mild inflammation with edematous swelling. It is less like a true pharyngitis than like an involvement of the lymphatic tissue, the same tissue as in the lymph nodes.

Examination of the blood shows a definite leukocytosis; polymorphonuclears predominate at first and after a few days give way to lymphocytes, especially large ones, which persist for several months.

The period of incubation is about four days.

The children observed showed great susceptibility to the disease. The organism obtained by smear and culture was a gram-positive, weakly hemolytic diplostreptococcus.

GERSTLEY, Chicago.

THE EFFECT OF INHERITED CONSTITUTION IN COMMUNICABLE DISEASE. B. DE RUDDER, Monatschr. f. Kinderh. **48**:91, 1930.

As knowledge of the inheritance of constitution is too incomplete to attempt any judgment, information must be secured through the study of family epidemiology.

Points to be considered are: susceptibility and an increased resistance to such diseases as measles and scarlet fever; the course and severity of these diseases: repeated attacks of the same disease; numerous deaths in the same family from the same disease, and especially virulent types of a certain disease occurring in the same family.

By a more searching family history the welfare stations could do much to reduce some of this unnecessary mortality by being warned in advance and taking more vigorous steps in prophylaxis and treatment at the onset of the infection.

GERSTLEY, Chicago.

THE INTRATHECAL INJECTION OF DIPHTHERIA SERUM. S. WOLFF, München. med. Wchnschr. **77**:681 (April 18) 1930.

The appearance of toxic symptoms, such as vomiting, anemia, arrhythmia and albuminuria, after the acute stage of a severe diphtheritic infection is a bad prognostic sign. In 1911 Bingel called attention to this "insidious diphtheritic poisoning"; he considered it the result of injury to the central nervous system. He suggested that the patients be treated by the administration of diphtheria serum

intrathecally by lumbar puncture. Wolff urges the use of this form of therapy in cases with a poor prognosis, especially in sections in which the mortality has been unusually high.

BRANDY, Mount Vernon, N. Y.

AN ACTIVE SCARLET FEVER EXTINCTION PHENOMENON. H. HENTSCHEL, Ztschr. f. Kinderh. **49**:205, 1930.

In five cases of scarlet fever there occurred more or less round extinctions of the rash, about the size of a mark, which were typical of the extinction phenomenon of Shultz-Charleton. In all the cases there was a history of impetigo and in two cases there were fresh lesions, around which the extinction likewise appeared. Hentschel would like to call this phenomenon "active extinction." He thinks that some kind of streptococcus antitoxin led to this active immunization, and in consideration of the hemorrhagic nephritis that comes with or after impetigo, which resembles the nephritis of scarlet fever, he believes that it is a reaction to a similar poison.

EMERSON, Boston.

DENGUE FEVER IN INFANTS. NICOLAS J. SPYROPOULOS, Acta pædiat. **10**:59 (Aug. 18) 1930.

In the course of an epidemic of dengue fever in Greece in 1928, the author observed a number of cases in infants and children. The youngest patients were only 8 or 10 days of age. No special age incidence was observed. The disease set in usually with fever, sometimes also with general malaise and vomiting, and in young infants occasionally with convulsions. After the initial rise to from 38 to 40 C. (100.4 to 104 F.), the temperature usually fell gradually in from three to six days in older children, and in from two to four days in infants under 1 year of age. Afebrile forms were rare. After an inconstant prodromal rash, usually a simple erythema, the eruption of the disease itself appeared first on the extensor surfaces of the hands and arms and then spread to the rest of the body; sometimes it was scarlatiniform and at other times morbilliform or roseolar. The prominence of the eruption bore no relation to the severity of the attack. As a rule the eruption appeared first after from one to three days of fever; in rare cases it was found only after defervescence. Itching and desquamation were rarely found. Pain in the muscles, headache and arthralgia, which were mild in the older children, could not be detected in infants; on the whole the disease was far milder and had a lower mortality than in adults. A leukopenia of from 4,500 to 6,000 was the rule.

MCINTOSH, New York.

PROPHYLAXIS OF MEASLES WITH CONVALESCENT SERUM. O. BANG, Acta pædiat. **10**:98 (Aug. 18) 1930.

In a series of 152 patients given a prophylactic injection of the serum of patients convalescing from measles, the author observed complete protection in over 88 per cent, while attenuated forms of the disease developed in an additional 9 per cent.

The serum used is collected on from the seventh to the tenth day after defervescence; it is pooled and prepared in the usual way, and administered within the first four days of exposure. The dose is 5 cc. for infants up to 1 year of age, 10 cc. for infants from 1 to 3 years of age and 15 cc. for all others.

No information was obtained regarding the duration of passive immunity in the patients completely protected. An analysis of the failures suggests that the serum of convalescent patients has a relatively weak protective power in the presence of whooping cough in patients under 1 year of age, and of scarlet fever in those over 1 year.

MCINTOSH, New York.

THE POLYMORPHISM OF HEMATOGENIC MILIARY TUBERCULOSIS OF THE LUNG. H. T. DEELMAN, Nederl. tijdschr. v. geneesk. **74**:1584 (March 29) 1930.

The author points out the polymorphism that tubercles in miliary tuberculosis of the lung often show. The differences are not only in the size of the tubercles, but also in their number and their histologic structure. In a special study the author found that not only are there differences in the time of development of histologic structure (young and old tubercles), but the character of this development changes. One can distinguish the tubercles with a more exudative, and those with a more productive, character. In the productive tubercles an increase of mesenchymal cells and their derivatives takes place. The resistance of the patient against the disease usually determines the kind of tubercles that appear; a strong resistance gives rise to productive forms and a less strong resistance to exudative tubercles. Mixed forms, in which the productive type surrounds the exudative type, are not rare. In such cases one must conclude that during the development of the tubercles the process of inflammation of exudative origin has become productive at the margin of the tubercle. This also means that during the course of the disease an increase in the resistance of the organism has taken place, giving rise to a more productive inflammatory process as opposed to the exudative process. The author illustrates his opinion by several observations and concludes that the changes in the histologic structure of the tubercles described gives an idea of the struggle that occurs between the body and the virus even in miliary tuberculosis. The body would perhaps more often win were it not for the fact that a complicating meningitis often causes death. These observations on the tubercles give a new significance to the fact that recovery from miliary tuberculosis frequently occurs.

VAN CREVELD, Amsterdam, Holland.

EFFECT OF SERUM IN SCARLET FEVER. E. J. M. BELINFANTE, Nederl. tijdschr. v. geneesk. **74**:2865 (June 7) 1930.

The author gives the results of serum therapy in scarlet fever in the department for infectious diseases of the Wilhelmina Hospital in Amsterdam. Patients were selected who had no severe toxic symptoms (a temperature higher than 40 C. [104 F.] and the appearance of extreme illness, dulness, confusion and disorder) and whose temperature on the second day was still higher than 39 C. (102.2 F.). Half of these patients (about 100) received serum; those less than 3 years of age were given 25 cc., and older children 50 cc.). The direct influence of the serum was studied next, as to its effect on the complications and as to the appearance of serum exanthems. The effect of the injection was not so convincing as would be expected from the publications of other investigators. The impression was obtained, however, that there was some effect on the temperature and general condition. Little or no influence of the serum was seen on the complications that appeared later. The use of antiscarlet-fever serum is strongly recommended in toxic cases. Serum therapy is not recommended in the average case of scarlet fever because the patients are made anaphylactic by it and also because of the serum exanthems.

VAN CREVELD, Amsterdam, Holland.

TWO CASES OF IRITIS ASSOCIATED WITH MUMPS. V. POPOVICI, Viata med. **5**: 56, 1929.

Seven cases of iritis—iridocyclitis following epidemic parotitis—are said to have been published in the literature. The author describes two such observations, one in a girl aged 8 years and one in a woman aged 20. The iritis began from four to five days after the mumps had begun. The nature of the disease was benign. Therapy consisted of instillations of atrophine and intravenous injections of neoarsphenamine.

BLATT, Tagu-Mures, Roumania.

Chronic Infections

A Study of the Provocative Wassermann, Kahn and Vernes Flocculation Tests for Syphilis on Identical Specimens of Serum. Morris A. Lyons, Am. J. Syph. **14**:366 (July) 1930.

The author's summary is as follows: "The serologic studies following the provocative procedure demonstrated that the Vernes flocculation test is more often positive than the Kahn test or the Wassermann test. A single serologic examination following the provocative procedure was found misleading. In view of the discordant results, more than one test for syphilis is necessary following the provocative procedure."

Royster, University, Va.

The Effect of Ultraviolet Radiation on Tuberculous Peritonitis in Guinea Pigs. M. Maxim Steinbach, Alfred F. Hess and Mildred Weinstock, Am. Rev. Tuberc. **22**:35 (July) 1930.

The authors conclude from experimental work that when guinea-pigs are infected with mildly virulent tubercle bacilli intraperitoneally, extensive tuberculous disease develops, even though the animals are subsequently treated with ultraviolet radiation. In three series of tests, tuberculosis developed to fully the same degree in the irradiated animals as in those which had not been treated with ultraviolet rays; in some instances the treated animals showed more extensive disease than did the controls.

Smith, Ogden, Utah.

Diagnosis and Treatment of Yaws. C. S. Butler, Internat. Clin. **2**:1 (June) 1930.

A detailed argument defending the identity of epidemic syphilis and "yaws" is presented. Yaws is defined as "epidemic non-venereal syphilis transmitted innocently among primitive peoples, and under stone-age conditions of personal hygiene constitutes one of the exanthemata of childhood." Synonyms are frambesia, pian, bubas, etc. In Haiti, 90 per cent of the population is estimated to be infected. Symptoms quickly disappeared under antisyphilitic treatment.

Miller, South Bend, Ind.

Tuberculosis and Uncinariasis: An Analysis of Sixty-Eight Cases. C. DeWitt Colby and K. Schaffle, South. M. J. **23**:801 (Sept.) 1930.

With the exception of three "resort states" in which high rates were due to imported cases, there is more tuberculosis in the South than in any other section of the United States. Hookworm disease is also widely prevalent in spite of two decades of organized effort toward eradication.

The authors report sixty-eight cases, in forty-three of which both diseases were present. There were twenty-five cases of uncinariasis that had been referred with a diagnosis of tuberculosis.

Ferric sulphate is efficient as a vermifuge for hookworm, whip worms and round worms; it is safe and causes no discomfort in the treatment of weak and emaciated persons.

Schlutz, Chicago.

Two Years Experience of the Kahn Reaction. D. S. Murray, Lancet **1**:1344 (June 21) 1930.

Absolute disagreement between the Wassermann and Kahn tests was found in 2.43 per cent of the patients tested by Murray. In a large number of treated patients the Kahn reaction remained positive after the Wassermann reaction had become negative.

Langmann, New York.

SYPHILITIC CIRRHOSIS OF THE LIVER IN A BOY. DAVID NABARRO, Proc. Roy. Soc. Med. **23**:1103 (June) 1930.

A case of syphilitic cirrhosis of the liver was reported in a boy aged 11 years and 9 months. The patient had snuffles at birth and received the usual treatment with mercury. In 1927, he complained of pain in his right side. The liver then was hard and nodular. The Wassermann reaction was strongly positive. He responded somewhat to antisyphilitic treatment. Later he was given further treatment with no further response. The Wassermann reaction was still strongly positive. Malarial therapy was begun, but affected him so severely that quinine was used to cut short the attack.

WILLIAMSON, New Orleans.

PULMONARY ACTINOMYCOSIS IN CHILDREN. P. NOBÉCOURT and M. KAPLAN, Arch. de méd. d. enf. **33**:391 (July) 1930.

Although the parasite, *Actinomyces bovis*, was not described in detail until 1877, unrecognized cases of its ravages in man were reported by Robin in 1812 and by Laboulbene in 1853. In 1878, Israel published a brief review of two cases in which the typical yellow granules were found, and further contributions were made by Nocard, Lucet, Poncet and Berard.

At present, several varieties of the organism are known, the most important one, from a medical standpoint, being *Actinomyces hominis*. The disease is encountered in every country, but must be considered rare; its chief localization is in the head or neck, but it may attack other organs or tissues. In a review of 1,009 cases, Laederich found the lungs to be invaded in 14.76 per cent, the intestines in 18.05 per cent and the limbs in 2.37 per cent, while the head and neck bore the brunt of the attack in 62.25 per cent. In a further statistical study made by the American observers, Huber and Berkowitz, comparable figures were reported.

Actinomycosis is excessively rare among children. Of 670 cases reported in the United States, only 42 (6.26 per cent) occurred in persons under 15 years of age; 5 of these showed pulmonary involvement. The authors report a case of actinomycosis of the lungs in a girl, aged 14, still under treatment with potassium iodide and roentgen rays.

AMESSE, Denver.

TUBERCULOSIS IN INFANCY. D. DELCOMINETTE and A. LEMALLE, Progrès méd., Sept. 20, 1930, p. 1553.

This article is taken from the report of the International Association for the protection of infancy at Liége in 1930. Tuberculosis in children is rarely hereditary; it is almost always acquired. The contagion is usually from the immediate family. Few cases are acquired from other sources. The bovine bacillus is rarely the source of infection, at least in Belgium and France. While it is important to remove tuberculous persons from the proximity of children, the best results will be obtained by propaganda in the schools and by frequent physical examinations.

SANFORD, Chicago.

PROHPYLAXIS OF CONGENITAL SYHILIS. A. COUVELAIRE, Rev. internat. de l'enf. **9**:500 (June) 1930.

Two general methods are presented for the elimination of heredosyphilis: one through radical eugenics, which seeks to prevent procreation by infected persons or the actual sterilization of persons with syphilis, and the other by means of treatment.

The author advocates intensive treatment of prospective parents whenever doubt exists, and the continuous treatment of an infected mother throughout pregnancy. The treatment should be continued in the new-born infant until reason-

able assurance of good health is offered. By such methods, the fetal mortality has been reduced from 75 to 5 per cent in recent years. Adequate management is not a matter of weeks but of years.

AMESSE, Denver.

THE INFLUENCE OF INSULIN ON THE PROTEIN EXCHANGE IN CHILDREN WITH PULMONARY TUBERCULOSIS. E. M. MONDINI, Pediatria **38**:483 (May 1) 1930.

The author studied the behavior of the protein exchange in children suffering from inactive or moderately febrile pulmonary tuberculosis who were treated with insulin. In each case he obtained a febrile reaction, and in one case also an active local reaction, with the administration of the drug.

The protein exchange was unfavorably influenced, the nitrogen balance being markedly decreased. Mondini believes that the increased consumption of the protein observed has some connection with the rise in the temperature and also with a direct action of the insulin on the protein exchange.

SIGNORELLI, New Orleans.

THE FIFTH CASE OF LEISHMANIOSIS VISCERALIS OBSERVED IN SARDINIA. A. GUALDI, Pediatria **38**:834 (Aug. 1) 1930.

The author reports his fifth case of leishmaniosis visceralis observed in Sardinia, and directs attention to the fact that this disease may be more prevalent than ordinarily supposed, and that it is sometimes confused with malaria.

He stresses the importance of early diagnosis, and directs attention to the dog as the host of the organism and the flea and bedbug as the transmitting agents. He points out the frequency with which adults are infected and recommends as the best mode of treatment, the persistent administration of moderate doses of tartrated antimony.

SIGNORELLI, New Orleans.

CURE IN TUBERCULOUS MENINGITIS. B. DE LUCA, Riv. di clin. pediat. **28**:663 (Aug.) 1930.

The author reports a case in a boy, aged 10 years, in whom tuberculous meningitis developed. The clinical symptoms and signs were headache, drowsiness, hypertonicity, a positive Kernig sign and enlarged lymph glands. Lumbar puncture showed the spinal fluid to be under slightly increased pressure; the fluid contained an increased number of cells, mostly lymphocytes; a film formed. Tubercle bacilli were found in the smear. Fluid was injected into a guinea-pig; the animal was killed two months later and found to have caseous tuberculous inguinal and retroperitoneal glands. After ten days, the child began to improve; he was discharged from the hospital one month later. When last observed, he had remained well for one year.

HIGGINS, Boston.

NEUROPATHIC MANIFESTATIONS IN CONGENITAL SYPHILIS IN CHILDREN. V. MIKULOWSKI, Scritti medici dedicati a Carlo Comba, ediz., Riv. di clin. pediat., 1929, p. 43.

A girl, aged 13 years, had had abdominal pains, at intervals since she was 1½ years of age. One year previous to examination, she had undergone appendectomy which had failed to relieve the condition. Physical examination revealed a sympathetic otonia, a cessation of growth and a tendency to obesity. Her blood showed a positive Wassermann reaction. With antisyphilitic treatment, the pains ceased and a cure was brought about.

HIGGINS, Boston.

LOCAL AND GENERAL TUBERCULOSIS FOLLOWING RITUALISTIC CIRCUMCISION. R. FISCHL, Scritti medici dedicati a Carlo Comba, Riv. di clin. pediat., 1929, p. 58.

The author found in the literature sixty-nine cases of tuberculosis following and traceable to ritualistic circumcision. Most of the cases were observed in Russia; lay operators affected with pulmonary tuberculosis were usually responsible.

The author feels that ritualistic circumcision is dangerous because of the age of the child (8 days), the method of operation, the defective antisepsis and the poor technic; he is of the opinion that it should be forbidden by law.

HIGGINS, Boston.

A CASE OF VIRULENT HEREDITARY SYPHILIS IN THE SECOND GENERATION. UGO DI GIRONCOLI, Scritti medici dedicati a Carlo Comba, ediz., Riv. di clin. pediat., 1929, p. 69.

The grandmother of a woman observed had contracted syphilis from her first husband. By her second husband, she had three children, two of whom seemed well, while the youngest had an uncertain neurologic condition. The oldest daughter married a healthy man and gave birth to a premature infant with definite syphilis (syphilitic pemphigus), as proved by a dark-field examination. The child responded well to antisyphilitic treatment. The mother showed no sign of hereditary or acquired syphilis; she had a positive Wassermann reaction. The father said that he had not had syphilitic infection; he gave no family history of syphilis, and he had a negative Wassermann reaction.

HIGGINS, Boston.

EXPERIMENTAL STUDY ON THE ACTION OF B C G GIVEN BY THE INTRACEREBRAL ROUTE. ENRIQUE M. CLAVEAUX, LOUIS J. MURGUIA and CLEMENTE ESTABLE, Arch. argent. de pediat. **1**:189 (May) 1930.

B C G injected intracerebrally in smaller doses than 0.0005 Gm. has no pronounced pathogenic action. If given to rabbits in larger doses by the same route, it produces death in over 60 per cent.

The dominant clinical symptom in the disease picture is malnutrition and cachexia. Anatomically there is leptomeningitis with round cell infiltration, alteration of the cells of the pyramidal tract and the formation of a typical follicle of the epithelial cells.

The disease picture seems to depend on a tuberculous impregnation of the nervous system and seems to be the picture of the ultravirus of tuberculosis.

SCHLUTZ, Chicago.

A TUBERCULOUS CAVITY IN INFANCY. E. FILGUEIRAS, Arch. de pediat., Rio de Janeiro **2**:670 (July) 1930.

A child, aged 14 months, had suffered with a catarrhal disturbance and failure to gain for some time. The temperature was 36.8 C. (98.2). Physical examination disclosed peribronchial glands and a restricted area of breathing in the upper lobe of the right lung, surrounded by subcrepitant râles. A roentgenogram disclosed a large cavity.

SANFORD, Chicago.

B C G IN URUGUAY. J. A. BAUZA, Arch. pediat. d. Uruguay **1**:287 (June) 1930.

The author presents the results of vaccination with B C G vaccine in the Welfare Clinic of the Casa del Niño during the past 3 years. B C G vaccine was given by the oral route according to the method of Calmette. Of the infants studied, 197 were followed for more than 1 year. No unfavorable action could

be observed in a single case. The general mortality of this group was not influenced by the vaccine and was about the same as that in an equally large group of children who had been observed 2 years previously but who had not been vaccinated.

In sixty cases the Pirquet reaction was found to be positive in 30 per cent, whereas a positive intradermal reaction was obtained in 56.2 per cent, including patients who had given a negative Pirquet reaction. In the sixty cases observed, twenty-nine positive reactions were obtained during the first and second year of life. This represented 65 per cent.

The author is of the opinion that the vaccine given by the oral route is harmless, but he expresses some doubt as to whether it is entirely effective if given this way. Revaccination of infants over 1 year of age and vaccination of infants under 10 days can be accomplished without danger of causing tuberculosis; the subcutaneous method may be used. The dosage used should not exceed 0.2 mg., or the equivalent of 800,000 bacilli.

In the author's opinion, B C G vaccine should be given to all children in a tuberculous environment or in one where hygienic measures are deficient.

He is not prepared to say with certainty that all the vaccinated children obtained complete immunity to tuberculosis, but he points out that the time that has elapsed since the beginning of this study has not been sufficiently long.

SCHLUTZ, Chicago.

DEFORMING DISEASE OF THE STOMACH IN A CHILD WITH CONGENITAL SYPHILIS. H. G. HUBER, Ztschr. f. Kinderh. **49**:179, 1930.

A boy, aged 8½ years, was well, except for frequent attacks of ocular inflammation, until he began to vomit daily; it was thought for a time that the condition was caused by the death of a beloved grandmother. On the basis of a hereditosyphilitic bilateral fistula of the tear sacs, the "pepper and salt" appearance of the eyegrounds, a positive Wassermann test in both the patient and his father, vomiting uninfluenced by dietetic or medical treatment, marked hypo-acidity or anacidity, occult blood in the stool, an irregular temperature curve, roentgen observations on the stomach indicative of late disease in congenital syphilis, the patient was treated for the latter condition and became practically well.

EMERSON, Boston.

COLLATERAL INFLAMMATION OF THE LUNG AROUND A TUBERCULOUS CENTER. E. GORTER and G. O. E. LIGNAC, Acta pædiat. **10**:187 (Aug. 18) 1930.

A girl, aged 3 years, with a history of prolonged exposure to tuberculosis, was admitted four weeks after an attack of measles, having had a cough and intermittent fever since the onset of the illness. There was marked dulness at the apex of the right lung, with bronchial breathing and a dense shadow shown roentgenologically. Needle exploration yielded no free fluid, but from the small quantity of material obtained both tubercle bacilli and pneumococci type II were recovered. There was gradual clinical improvement, although the lungs did not clear entirely. A year and a half after the aforementioned episode the apparent improvement unexpectedly terminated in an attack of tuberculous meningitis, from which the patient died.

In the right lung the apex was bound by dense fibrous adhesions and there was a partly calcified caseous focus in the anterior part of the upper lobe. In the hilus of the left lung there was a single tuberculous lymph node. No tubercles were visible macroscopically, however, either in the lymph nodes of the right lung or at the bifurcation of the trachea. There was tuberculosis of the kidneys, prevertebral lymph nodes and meninges.

The authors regard the original extensive pulmonary involvement as a tuberculous pneumonia complicated by pneumococcal infection.

MCINTOSH, New York.

THE ROENTGENOLOGIC DIAGNOSIS OF TUBERCULOSIS OF THE BRONCHIAL GLANDS. G. J. HUËT, Nederl. tijdschr. v. geneesk. **74**:3424 (July 5) 1930.

The author illustrates why roentgenograms in the frontal position, even when the technic is good, may be unsatisfactory for the diagnosis of tuberculosis of the bronchial glands. Before excluding this diagnosis, a lateral roentgenogram is necessary.

VAN CREVELD, Amsterdam, Holland.

Internal Diseases

BRONCHIAL ASTHMA IN CHILDREN. J. A. CLARKE, JR., and EDWARD F. BURT, Arch. Pediat. **47**:337 (June) 1930.

The authors describe the routine measures in the asthma clinic of Jefferson Hospital, Philadelphia, and give the results in 220 children. They feel that there are the following differences between asthma in children and that in adults: (1) a higher percentage with positive skin reactions, (2) a lower percentage with continuous dyspnea and (3) a better prognosis.

Asthma that appears after colds is frequently allergic in origin and is easily relieved by appropriate treatment.

WADDELL, University, Va.

PRIMARY HYPERTENSION IN CHILDHOOD: THE INFLUENCE OF HYPERSUPRARENALISM. ALVIN E. SIEGEL and PHILIP C. THOMAS, Arch. Pediat. **47**:473 (Aug.) 1930.

Most references to hypertension in infancy and childhood are concerned with hypertension secondary to renal and cardiovascular conditions.

A case of primary hypertension in a child of endocrine type is reported. In the supposition that the hypertension was the result of hyperadrenalism, 1 cc. of a 1:1,000 solution of epinephrine was injected. This resulted in a marked rise of the blood sugar curve, which was maintained. A similar test in a control child gave a sharp rise in the blood sugar level, followed by a rapid decline to normal. Siegel and Thomas are of the opinion that the hypertension in this case was the result of the excessive secretion of epinephrine.

WADDELL, University, Va.

NEPHROPATHIES. MARK S. REUBEN, Arch. Pediat. **47**:482 (Aug.) 1930.

A thirty page article on the nephropathies is presented, which does not lend itself to profitable abstracting.

WADDELL, University Va.

A STUDY OF THE RARE HUMAN TAPEWORM, TAENIA CONFUSA, WITH A REPORT OF THE FOURTH CASE. ERNEST CARROLL FAUST, South. M. J. **23**:902 (Oct.) 1930.

The case of infestation with *Taenia confusa* reported was of more than eleven year's standing. It occurred in a native white woman of Louisiana. The author believes that it is the fourth case reported. The parasite seemed to be similar to *Taenia saginata*. Raw beef seemed to be the source of the infection. Infection with the worm occurs more often than is supposed.

Six cubic centimeters of oleoresin male fern was given, 2 cc. at fifteen minute intervals; thirty minutes after the last dose, a magnesium sulphate purge was administered. This treatment seemed to effect a permanent cure.

SCHLUTZ, Chicago.

INSTITUTIONAL INFECTIONS AND PROPHYLACTIC COLD VACCINES. F. R. JANNEY, Wisconsin M. J. **29**:205 (April) 1930.

Nonmedical institutions (orphan homes, etc.) have a heavy morbidity from contagious diseases and respiratory infections, due largely to ignorance about the

control of contagion. State supervision will need to be more vigorous in order that institutions of this kind are more intelligently managed from the medical point of view.

In a series of thirty institutional children given a standard mixed cold vaccine and observed over eight months, the older children had apparently fewer respiratory infections than did the controls. Those under 3 years of age showed no benefit.

JANNEY, Milwaukee.

GENITODYSTROPHIC GERODERMA. A. BARDISIAN, Riv. di clin. pediat. **28**:457 (June) 1930.

Geroderma (genitodystrophy) was first clearly described by Rummo and Ferranini in 1897. The author reports a case of this condition in a boy, aged 14 years. The child was normal until he had influenza at the age of 6 years; since then the symptoms had gradually developed. The distinctive observations were: (1) his extreme emaciation (adipose tissue was absent); (2) his senile appearance, wrinkles being present; (3) the angularity of the bones of the face and epiphyses; (4) the mild degree of hypospadias, and the small and soft testes; (5) the complete absence of hair from the suprapubic region, the axilla and the upper lip; (6) the small heart, and (7) the enlargement of the sella turcica, as shown roentgenologically.

The author believes that the condition was caused by pluriglandular lesions. The child did not remain under observation for treatment. He died one year later of a cause unknown to the author.

HIGGINS, Boston.

CLINICAL CONTRIBUTION TO THE STUDY OF INFANTILE ACRODYNIA. L. GREPPI, Riv. di clin. pediat. **28**:597 (July) 1930.

The author reports eleven cases of acrodynia in children, nearly all of them occurring in or near Novara during 1928 and 1929. In several of the patients, changes were found in the spinal fluid; there was globulin present and a cell count of from 38 to 130. Greppi studied the relationship between the rectal and skin temperatures.

Acrodynia has much in common with epidemic encephalitis; it is an epidemic infection involving the nervous system. It may be grouped among the "paraencephalitides" of Sicard and Economo.

HIGGINS, Boston.

CLINICAL AND ANATOMICOPATHOLOGIC CONTRIBUTION TO THE KNOWLEDGE OF RENAL TUMORS IN CHILDREN. A. CARDIA and G. CAREDDU, Riv. di clin. pediat. **28**:649 (Aug.) 1930.

The authors report a case of a tumor of the kidney in a child, aged 1½ years. It was several months after the swelling was first noticed that the child showed clinical or urinary symptoms. During the operation to remove the tumor the patient died.

The tumor was shaped like a watermelon and weighed 850 Gm.; the authors believe that it was a perithelioma tous sarcoma.

HIGGINS, Boston.

MALIGNANT TUMORS AND EOSINOPHILIA; RARE SARCOMA OF THE SKULL. A. BARDISIAN, Riv. di clin. pediat. **28**:802 (Sept.) 1930.

A patient, aged 32 months, had two tumors on the right side of the head, one above and in front of the ear and the other above the eye. They grew slowly having first been noticed when the child was 15 months of age. The mother felt that the tumors tended to diminish in size when there was a discharge from the nose and ear. The tumors gradually increased in size, one becoming the size

of a walnut and the other the size of a hazelnut; they were rubbery in consistency. The child had a positive Wassermann reaction; antisyphilitic treatment did not affect the tumors. The blood count showed 11,500 white blood cells (43 per cent polymorphonuclears, 3 per cent eosinophils, 23 per cent lymphocytes and 21 per cent large mononuclear cells).

A roentgenogram of the skull revealed rarefaction beneath the tumors. A biopsy was performed. The tumors proved to be sarcomas; however, there were an unusually large number of eosinophilic cells in the tumor tissue. This is not common and is usually regarded as a good prognostic sign, in that the tumor will not spread rapidly and will probably respond to actinic therapy.

HIGGINS, Boston.

A LITTLE KNOWN PHENOMENON IN PNEUMONIA IN CHILDREN. A. F. CANELLI, Scritti medici dedicati a Carlo Comba, ediz., Riv. di clin. pediat., 1929, p. 32.

Weill's sign depends on the complete or partial failure of expansion of the thorax in the subclavicular region on the side where there is pneumonia; it may be detected by inspection, by palpation or preferably by a written record (sphygmograph) of the respiration. The record is obtained by attaching threads to the skin of the chest with a piece of wax, the threads being connected to recording levers; a comparison of the records of the two sides of the chest affords a means of diagnosis. Weill's sign is present whether pneumonia is apical, medial or basal.

The author presents several cases in which Weill's sign was of value in diagnosis. One was a case of suspected tuberculous meningitis, which turned out to be lobar pneumonia. Another occurred in a child with apparent clinical pneumonia; localization was made by this sign.

HIGGINS, Boston.

RUPTURE OF A BRONCHUS WITH SUBCUTANEOUS EMPHYSEMA FROM TRACHEOBRONCHIAL ADENOPATHY. F. ROSSI, Scritti medici dedicati a Carlo Comba, ediz., Riv. di clin. pediat., 1929, p. 78.

In a child, aged 2½ years, signs suddenly developed that suggested bronchopneumonia: high fever, dyspnea and a barking cough. Two days later, subcutaneous emphysema appeared, extending from the neck to the abdomen. The child was very sick for one week and had an elevated temperature for one month. The signs of pneumonia were at the base of the left lung.

A roentgenogram made early in the illness showed the shadow of a large bronchial lymph gland on the left side; this was not present in the roentgenogram taken at the end of the illness.

The author made a diagnosis of rupture of a broken-down lymph gland into a bronchus, with resulting bronchopneumonia and subcutaneous emphysema. The tuberculin test was negative.

Two years later the child was doing fairly well.

HIGGINS, Boston.

PANCARDIAL TUMOR DUE TO SARCOMA OF THE MEDIASTINUM. J. G. FERNANDEZ, M. A. CARRI and L. RECARREN, Arch. argent. de pediat. 1:174 (June) 1930.

A pancardial tumor occurred in a boy, aged 11 years, and was due to a massive sarcoma of the mediastinum which had invaded both the pericardium and the wall of the heart.

A swelling in the precordial area, precordial pain and cough were the earliest symptoms observed. The duration of the disease from onset to fatal termination was about five weeks.

SCHLUTZ, Chicago.

PNEUMONIA OF THE AZYGOS LOBE. FRANZ HEPNER, Monatschr. f. Kinderh. **47**:311 (July) 1930.

The author reports a case of pneumonia involving the azygos lobe. He found it in 1 of 30,000 roentgenograms of the chest.

GERSTLEY, Chicago.

AN UNUSUAL BONE DISEASE IN INFANCY. GEORG ROSKE, Monatschr. f. Kinderh. **47**:385, 1930.

A boy, aged 7 weeks, was taken ill with swellings in the long bones and also in the lower jaw. The growths were tender. The blood count showed a leukocytosis with an increase of lymphoid elements. Roentgenography and later a biopsy revealed the lesions to be localized in the periosteum. Microscopic examination showed nothing definite. Tests for syphilis and tuberculosis were negative. The disease did not interfere with the child's health, and it disappeared spontaneously after about six months.

Roske thinks that the lesions may have been associated with some disturbance in the blood-forming tissues.

GERSTLEY, Chicago.

THE EOSINOPHIL CURVE AFTER INJECTION OF SERUM IN EXUDATIVE DIATHESIS. ALEXANDRINE STROBL, Monatschr. f. Kinderh. **47**:401, 1930.

This study confirms the author's previous observation that following injections of from 0.5 to 1 cc. of serum in normal subjects there is an increase of eosinophils lasting for forty-eight hours, while in the child with exudative diathesis the increase of eosinophils does not develop until after forty-eight hours. She shows a series of curves demonstrating that children with chronic eczema (four cases) show this reaction. In seven cases of tonsillar hypertrophy the reaction was negative. It was negative in two children with bronchitis, while it was positive in three with bronchiectasis, two of whom showed skin manifestations. It was negative in two children with scrofula.

GERSTLEY, Chicago.

DETERMINATION OF THE SIZE OF THE HEART IN CHILDHOOD BY X-RAYS. F. VON BERNUTH, Monatschr. f. Kinderh. **48**:25, 1930.

The author has not been satisfied with many of the methods of cardiac examination because they do not take into consideration the configuration of the heart in relation to the body as a whole.

He used x-rays at a distance of 1.5 meters. While he admits that orthodiagrams are more accurate, he finds them impossible to obtain in infants.

In trying many different measurements he came across an interesting series of relationships. Apparently the body length multiplied by the greatest transverse diameter of the lungs, taken usually at the level of the insertion of the diaphragm, divided by the transverse diameter of the heart gives a constant figure. This "constant," as he calls it, varies between 31 and 47, with an average of 39. If it is below 31 the heart is abnormally large; if it is over 47, the heart is especially small.

GERSTLEY, Chicago.

ALLERGY AND PARALLERGY. HANS FERNBACH, Monatschr. f. Kinderh. **48**:35, 1930.

The author reviews a former publication of Moro who found that certain patients gave positive tuberculin reactions to a certain glycerin bouillon.

Fernbach attempts to show that there is a class of patients who are parallergic; i. e., they give positive reactions to the peptones in the bouillon. Such reactions must be ruled out before a positive Pirquet reaction can be interpreted as evidence of a tuberculous infection.

In the discussion following this paper, considerable skepticism was expressed; the majority thought that the positive reactions with glycerin bouillon might be explained by the possible presence of a minute quantity of tuberculin in the bouillon.

GERSTLEY, Chicago.

A METHOD FOR THE DIAGNOSIS OF ADHESIVE PERICARDITIS. M. HOCHREIN, München. med. Wchnschr. **77**:588 (April 4) 1930.

Adhesive pericarditis occurs much more frequently than it is diagnosed. As an aid in the clinical diagnosis Hochrein uses a pneumotachograph which records the respiratory movements. In some patients observed, the only evidence of pericarditis was the characteristic curve obtained with the pneumotachograph. In several cases the diagnosis was confirmed by postmortem examination.

BRADDY, Mount Vernon, N. Y.

A CASE OF FOREIGN BODY IN THE INTESTINE, REMARKABLE FROM THE POINT OF VIEW OF DIFFERENTIAL DIAGNOSIS. KURT SCHIRLITZ, Ztschr. f. Kinderh. **40**:194, 1930.

A girl, aged 2 years, of the neuropathic type, had the habit of swallowing thread. An illness developed which closely resembled peritoneal tuberculosis; there was emaciation, vomiting, pain in the abdomen and a palpable mass, but no fever. The symptoms were all the more misleading because the history was incomplete. One thread was seen in the wash water of the stomach, but was disregarded. The child was operated on and died. In the jejunum was 125 Gm. of woolen and linen threads.

EMERSON, Boston.

CHOLECYSTITIS IN CHILDHOOD. H. VOLLMER, Ztschr. f. Kinderh. **40**:200, 1930.

A boy, aged 6½ years, had mild pharyngitis fourteen days before admission to the hospital. On May 29, he vomited, but had no fever; on the following two days he was better. In the morning he was struck in the abdomen by a football with some force; in the afternoon he complained of pain in the abdomen and vomited four times. The temperature was 97.7 F. There was no distention or spasm; the pain was localized to the right side, and in the upper portion there was a cylindric tumor, sensitive to touch. Intussusception was suspected, and was confirmed by roentgenograms. The tumor disappeared after an enema, but was felt again the next day. The night had been restful. After a high enema the tumor again was lost. The pains continued, however; there was a marked leukocytosis and the temperature was subfebrile. The diagnosis became uncertain. On operation, a tense injected gallbladder was found, containing 40 cc. of purulent fluid, which was sterile. Cholecystostomy was performed, but no stones were found. Recovery was accompanied by jaundice.

EMERSON, Boston.

CLINICAL STUDIES OF PERIARTERITIS NODOSA. GILLIS HERLITZ, Acta pædiat. **10**:105 (Aug. 18) 1930.

Of the 3 patients described, one was a girl aged 12 years, and the others were adults. In the child the disease was ushered in by an attack of sore throat with prolonged fever. In the second week she complained of dysuria, and the urine became dark. Fourteen days after the onset of the symptoms a flaccid paralysis of the right arm appeared, without sensory disturbance. The neck was stiff and the Kernig test positive. She was admitted to the hospital, where it was found that she had a clear throat, slight enlargement and tenderness of the cervical lymph glands, the neurologic signs described, pyuria, leukocytosis (28,800) and a normal spinal fluid. Two days after admission, circulatory changes suggestive of capillary emboli appeared in the extremities. The patient died seventeen days after the onset of pharyngitis. At autopsy, characteristic arterial changes were found in

the heart, spleen, kidneys, fingers and brachial plexus; there was an extradural hemorrhage in the region of the cervical swelling of the spinal cord.

Palpable changes in the peripheral arteries are found in only one eighth of all cases; one must, therefore, attempt the diagnosis without this clearcut sign; in fact, one should suspect periarteritis nodosa whenever the clinical picture of septicemia is complicated by flaccid paralysis. The elevation of temperature may be relatively slight; the pulse, on the other hand, may be rapid and thready in relation to the other signs. The patient is often strikingly feeble.

The organs most frequently involved are the heart and kidney, and the disease often terminates in death with symptoms referable to failure of these organs. Although many patients give a history of rheumatism, a direct etiologic relationship cannot be demonstrated. The cause remains obscure.

McINTOSH, New York.

PAROXYSMAL TACHYCARDIA IN AN INFANT. M. DE BRUIN, Nederl. tijdschr. v. geneesk. **74**:3415 (July 5) 1930.

Attacks of tachycardia were observed in an infant, aged 5 weeks. The roentgenogram and electrocardiogram were normal. Because of the symptomatology in other cases described in the literature and some symptoms which the child demonstrated, the supposition is made that the attacks of tachycardia were caused by encephalitis.

VAN CREVELD, Amsterdam, Holland.

AN ANTICOUGH MIXTURE. M. DMOCHOWSKA, Pedjat. polska **9**:180, 1929.

The author has great faith in medicinal fresh herbs, because many of these herbs were used successfully in olden times. Now, however, they are much neglected. The treatment with herbs is rapidly developing in England and France. The following cough mixture was used by the author:

(1) Drosera-rotundi flora (this has been used in conditions of the lung), (2) thymus vulgaris (known as an anticough remedy), (3) olei cupressi (used in cough mixtures in France) and (4) olei gamenoli-ex molalenca viridi flora (used in chronic coughs).

The author administered this remedy to children from 3 to 9 years old who had grip or whooping cough, and obtained satisfactory results. This illustrates that fresh medicinal herbs could be used successfully in treating patients for different diseases.

KRUPINSKI, Chicago.

Nervous Diseases

MANIC-DEPRESSIVE PSYCHOSIS IN IDENTICAL TWINS. ISABEL BRADLEY, Am. J. Psychiat. **9**:1061 (May) 1930.

Calling attention to the opportunity for investigation of the relative influence of heredity and environment offered by the study of personality traits in twins, Bradley presents an appropriate case. Her patients were identical twins. In one a manic-depressive psychosis developed at the age of 32, and in the other the first attack occurred five years later. Bradley believes that this case and others like it support the hypothesis that mental disease is dependent on hereditary defect in the germ plasm.

DAVIDSON, Newark, N. J.

TETANY OCCURRING IN IDENTICAL TWINS AT EIGHT WEEKS OF AGE. EDWARD D. ATLEE and RALPH M. TYSON, Arch. Pediat. **47**:513 (Aug.) 1930.

The authors report the simultaneous occurrence of tetany in identical twins 8 weeks of age. Treatment consisted of the usual antirachitic measures, and the administration of 3 units of parathyroid extract-Collip intramuscularly for seven days.

WADDELL, University, Va.

MENINGOCOCCUS MENINGITIS IN DETROIT IN 1928-1929. JOHN F. NORTON and JOHN E. GORDON, J. Prev. Med. **4**:207, 1930.

The present outbreak of meningococcus meningitis in Detroit began in the spring of 1928 and reached its peak in May, 1929. Although a rapid decline in the number of cases occurred during the summer of 1929, the morbidity rate was considerably above the norm up to the end of 1929.

The total number of cases reported from Jan. 1 to Dec. 31, 1929, was 867, and the number of deaths was 430, a fatality rate of 50 per cent. This percentage is higher than has been observed in most outbreaks since the introduction of modern methods of treatment (drainage of the spinal canal and treatment with serum). There is no reason to believe that the patients received treatment later than those in other epidemics. It must therefore be concluded either that the strain of meningococcus encountered was of unusual virulence or that the therapeutic serums available were not specific against this strain.

A study of the age, sex and color distribution of the cases shows that a high fatality occurred among infants and adults, that sex was of little importance and that the colored population accounted for more than its share of cases.

The distribution of cases in Detroit indicates that congestion of population was a minor factor in the outbreak.

[ARCH. PATH.].

THE SIGNIFICANCE OF THE PROTEIN CONTENT OF THE CEREBROSPINAL FLUID. F. T. GREY, Arch. Dis. Childhood **5**:187 (June) 1930.

The diagnostic value of the protein content of the cerebrospinal fluid is stressed. The results in 101 cases are given: 1. Fluids showing 0.04 per cent or less are normal. 2. Protein contents between 0.05 and 0.15 per cent indicate tuberculous meningitis. 3. Protein contents between 0.03 and 0.72 per cent show either pneumococcal or meningococcal meningitis.

KELLY, Milwaukee.

THE PATHOLOGY OF MEASLES ENCEPHALOMYELITIS. J. G. GREENFIELD, Brain **52**:171 (July) 1929.

Greenfield believes that it is necessary, for descriptive purposes, to separate a cerebral from a spinal form of postmeasles encephalomyelitis, although they are often combined. The cerebral form usually appears with a recrudescence of fever, in which somnolence or delirium and often convulsions are manifested. In almost every case the patient is soporous or even comatose. Definite signs of meningitic involvement are present. Papilledema is fairly common, and temporary amaurosis has been observed. This somnolent stage may pass off in a few hours, but can last a few days. A state of instability follows which is characterized by choreiform movements, or by naughtiness and bad temper. The patients usually recover from this stage in a few days, although a change in character can continue permanently. Cerebral or cerebellar focal sequelae may develop, but they are uncommon. The spinal type may be ushered in during a recrudescence of fever, but this does not always occur. Paralysis is usually confined to the lower half of the body and is associated with loss of sphincter control. As a rule the paralysis is flaccid, but tends to become spastic after the first forty-eight hours, with increase of deep reflexes and an extensor type of plantar response. The paralysis may be accompanied by a dissociated anesthesia in which pain and temperature sense is disturbed while touch remains intact. On the whole, examination of the cerebrospinal fluid is valuable only as a means of excluding other diseases rather than giving conclusive evidence of the presence of encephalomyelitis. Recovery, when it occurs, is usually remarkably complete. It is evident, therefore, that encephalomyelitis that occurs in some convalescent cases of measles must be regarded as a disease entity, distinct from epidemic encephalitis or Landry's paralysis.

The pathologic changes may be of three main types: (1) diffuse congestion of the brain, especially of the white matter, sometimes causing petechial hemorrhages, (2) discrete round cell, perivascular infiltration and (3) small unmistakably characteristic zones of demyelinization.

Neither clinical nor pathologic distinctions could be drawn between encephalomyelitis following measles and that which may follow vaccination for smallpox, while the epidemiologic incidence supports the similarity of the two diseases. It is therefore probable that these two conditions are caused by an unknown virus which spreads in epidemic waves, but which produces no disease unless stimulated to activity by the exanthematous disease.

BECK, Buffalo.

LATE FORMS OF FAMILIAL PROGRESSIVE MYOPATHY. K. H. KRABBE, J. Neurol. & Psychopath. **10**:289 (April) 1930.

Krabbe discusses the age incidence of the myopathies and points out that those which develop late usually do not present a familial history, while in 50 per cent of cases developing early in life, there is a familial history. He reviews about twenty cases from the literature that developed after the age of 30. In only two of these was there a history of similar conditions in the family. He reports two cases of his own, one in detail and one casually. The patients were sisters, and in both the condition developed at about 45 years of age. In both the condition was limited to the lower part of the legs; in one a biopsy was performed and showed a replacement of muscular by adipose tissue; Krabbe did not attempt to classify this case in any of the known groups.

ROBINSON, Kansas City, Mo.

A CASE OF DECEREBRATE RIGIDITY, WITH AUTOPSY. S. H. EPSTEIN and P. I. YAKOVLEV, J. Neurol. & Psychopath. **10**:295 (April) 1930.

The authors give a historic discussion of decerebrate rigidity and report a case. The case is that of a boy, aged 8, who was born after a long and difficult labor and who was cyanotic for six weeks. He had convulsions of two types from the time of birth until death. One type was a generalized tonic convulsion, while the other consisted of "crying spells" of a peculiar type. The first type was produced by excessive sensory stimulation — usually auditory — while the second was brought on by excessive manipulation. The four major points in the examination of the patient were: (1) attitude, (2) muscle tonus, (3) fits and (4) general and local motor reactions. These were similar to those described by other authors.

The pathologic examination showed various aplasias of the cerebrum and cerebellum, and an entire lack of the corpus callosum. Throughout the cerebrum, cerebellum and midbrain there was a paucity of ganglion cells, an increase of all glial elements and an increase of capillaries. The cortical layers of the cerebrum were not only deficient in ganglion cells, but the cellular architecture was greatly disturbed. The spinal cord showed little disturbance of the gray matter, but the corticospinal tracts were completely degenerated.

This case is of interest because it confirms clinically much experimental work on this subject.

ROBINSON, Kansas City, Mo.

HUNTINGTON'S CHOREA WITHOUT CHOREIFORM MOVEMENTS. DESMOND CURRAN, J. Neurol. & Psychopath. **10**:305 (April) 1930.

Curran reviews the semiology of Huntington's chorea without choreiform movements and reports carefully the condition and the family history of a patient observed. He points out a direct connection between the condition of the patient and that of other members of the family. Five other members of the family had this disease, including the patient's mother, and it was developing in one son of the patient. Except for dysarthria, there were no motor disturbances. The complaints were all objective mental disturbances. Curran concludes from the mental disturbances and the family history that the condition was Huntington's chorea.

ROBINSON, Kansas City, Mo.

CONGENITAL FACIAL DIPLEGIA. R. M. STEWART, J. Neurol. & Psychopath. **10**:317 (April) 1930.

Stewart discusses the literature of congenital facial diplegia and gives a short account of the symptomatology and concurrent defects. The pathology is discussed, but no attempt is made to explain the etiology. This description is transcribed from Heubner's report, and both the author and Heubner believe that this condition results from some slowly progressing disappearance of the nerve cells. A case is presented in which there were several other defects and a mental retardation that would place the case in the imbecile group. The claim is made that this is the only case on record of facial diplegia with mental retardation.

ROBINSON, Kansas City, Mo.

THE RORSCHACH TEST APPLIED TO DIFFERENT GROUPS OF CHILDREN BETWEEN 10 AND 13 YEARS OF AGE. MARGUERITE LOOSLI-USTERI, Arch. de psychol. **22**:51 (Sept.) 1929.

The author applied the Rorschach tests to three groups of children, a group from Zurich, one from Geneva and one from a foundling school. She found that the Zurich children (German extraction) were more infantile in their responses than the Genevese children (French extraction). Pupils in the foundling school were as a rule more infantile in their responses than children living in their own homes. If they showed neuropathic signs, however, they did not show this infantilism, but were more obstinate.

PEARSON, Philadelphia.

CONVULSIONS AND PILOMOTOR PHENOMENON. R. WAITZ, Bull. Soc. de pédiat. de Paris **27**:382 (July) 1929.

A male infant, weighing 4,630 Gm., was extremely cyanosed after a difficult labor. The heart beats were irregular. After a few minutes he took irregular gasps, and twenty-five minutes after birth the breathing began to be regular; five minutes later he cried aloud. He appeared normal for a period of eighteen hours after which he began to have spells of marked cyanosis and convulsions. During the convulsive seizures and sometimes between them the infant showed peculiar pilomotor phenomena. The hair of the scalp stiffered out like a brush while the skin on the face and limbs assumed the appearance of chicken skin. These pilomotor crises lasted from twenty seconds to two minutes after which the hairs assumed their normal aspect. The spinal fluid was bloody and the pressure was increased, higher during a convulsion than in the intervals between convulsions, and always increased even more during the pilomotor seizures whether these accompanied a convulsion or not. The infant died forty-four hours after birth. Postmortem examination showed peribulbar congestion, a hemorrhagic area under the tentorium cerebelli and congestion of the choroid plexuses. In this infant as well as in normal infants, one could not produce the pilomotor crises by the application of cold, ether or xylene to the skin or by the intradermal injection of epinephrine. The pilomotor musculature in this infant did not show abnormal development as compared with that of other new-born infants.

BENJAMIN, Montreal, Canada.

THROMBOSIS OF CAVERNOUS SINUSES IN AN INFANT. H. ESCHBACH, Bull. Soc. de pédiat. de Paris **27**:550 (Dec.) 1929.

A boy, aged 2 months, who had had loose stools almost since birth but who had gained weight, was taken ill suddenly with high fever. The following day both upper eyelids were swollen and edematous, more on the left than on the right side. The next day the lids were red, and there were lines of lymphangitis over the bridge of the nose, extending toward the left side of the forehead. From then until five days later, when the infant died, the condition grew steadily worse;

the left eye showed chemosis, a blue turgid vein coursed transversely across the left upper eyelid starting at the internal angle of the eye, exophthalmos appeared and the pupil became widely dilated. No portal of entry of the infection could be found. It was thought that the infant may have had a septicemia, possibly of intestinal origin, with a septic focus localizing in the cavernous sinuses. The only other condition considered in the differential diagnosis was a retro-orbital cellulitis; the appearance of edema of the eyelids at the onset is rather in favor of the diagnosis of thrombosis of the cavernous sinuses, more marked on the left than on the right side.

BENJAMIN, Montreal, Canada.

ETIOLOGY OF DEFICIENCY OF THE GLOSSAL REFLEX IN THE INFANT. PIERRE ROBIN, Bull. Soc. de pédiat. de Paris **27**:553 (Dec.) 1929.

The author adopts the term, reflex, to indicate the normal tone of the tongue. He notes that in the lower animals the tongue always protrudes after death, whereas the human being dies with the tongue fallen back on the pharynx. This led him to study the "glossal reflex" in the infant.

The difference in glossal tone between the lower animals and the human being is due to the adoption of the erect posture by the latter. In man's phylogenetic evolution the lower jaw has receded, the upper jaw has been shortened, and the change in the reflex support of the tongue has taken place to facilitate speech. The last developed morphologic functional change is the first to show any defect; infants with atresia of the mandible therefore present difficulty in nursing at the breast as well as in breathing and offer problems in rearing. When there is deficiency of the glossal reflex, the infant should be held at the breast with the thorax in the upright position; this causes stretching of the neck and pushing forward of the chin, which correct the deficiency. Pauses during the nursing period prevent fatigue, which is always accompanied by loss of glossal tone so that the tongue tends to fall back toward the vertebral column.

BENJAMIN, Montreal, Canada.

GLIOMA OF THE FOURTH VENTRICLE (MEDULLOBLASTOMA). CLAIRE VOGT and YVES BUREAU, Bull. Soc. de pédiat. de Paris **27**:556 (Dec.) 1929.

A boy, aged 8 years, showed two distinct periods in the course of the disease: (1) For a period of months he had periodic spells of vomiting, but the presence of tumor of the brain was not suspected; (2) later a number of symptoms appeared at the same time simulating an acute onset, e. g., peripheral pains referred to the nape of the neck and the shoulders (there was no headache during the entire course), holding the head to one side, ocular disturbances and urinary incontinence. The urine was normal.

Two points are emphasized: the production of complete bilateral optic atrophy in about fifteen days, and the evening rise in temperature to 38 C. (100.4 F.) during his first month of hospitalization, which suggests tuberculoma, but which is not rare during the development of glioma, more especially medulloblastoma. The patient died four hours after operation. Anatomic and histologic examination of the brain and the tumor are described.

Medulloblastoma is the most malignant of the gliomas. It is an embryonic form of glioma found practically exclusively in children. Surgical treatment, which should be attempted as early as possible, should be supplemented by roentgen therapy as this is the only type of glioma in the child which yields somewhat to roentgen therapy.

BENJAMIN, Montreal, Canada.

SPIROCHETAL MENINGITIS. J. TROISIER and Y. ROQUIEN, Presse méd. **38**:982 (July 19) 1930.

A case of meningitis due to the spirochete of Inada and Ido is reported in a dishwasher. He pricked his finger deeply, but continued to wash dishes and presumably infected himself from the water.

BIEKER, St. Petersburg, Fla.

CEREBROSPINAL MENINGITIS IN MOTHER AND CHILD. R. MACKINNON and MARIO RODELLA, Arch. de pediat. d. Uruguay **1**:427 (Aug.) 1930.

The authors report a case of cerebrospinal meningitis occurring simultaneously in an infant, aged 10 months, and its mother. The infant received four intraspinal injections of 15 cc. each of antimeningococcic serum. The mother was given the serum both intraspinally and intramuscularly and received a total of 180 cc. of the serum.

Both patients made a complete recovery. The infant was given artificial feedings.

SCHLUTZ, Chicago.

THE ETIOLOGY OF MONGOLIAN IDIOCY. A. BAUER, Arch. f. Kinderh. **90**:169 (May 24) 1930.

The author reviews two cases of mongolian idiocy personally studied in twins, and thirty-eight cases that he gathered from the literature. He does not believe that the usual idea of exhaustion of the mother plays any rôle in the development of mongolian idiocy, and in fact, does not consider any exogenic factor responsible. He reasons that otherwise the condition would always develop in both twins. This is not the case, however, in dizygotic twins. The author believes, therefore, that the cause of mongolian idiocy is genotypical and not paratypical.

SANFORD, Chicago.

THE PRESENT KNOWLEDGE OF NEUROSES OF CHILDREN. S. KATZ, Arch. f. Kinderh. **90**:216 (May 24) 1930.

The author discusses the subject of neuroses in children as presented by the various schools. She gives as the conceptions of present interest: the reflex (von Pawlow), the behavioristic (Watson), the individualistic (Jaensch), that of character and temperament (Kretschmer), the psychologic (Wiener) and that of individual psychology (Adler).

SANFORD, Chicago.

ENCEPHALITIC CHANGES IN DEHYDRATION. M. A. GOLDZIEHER, Klin. Wchnschr. **9**:981 (May 24) 1930.

The author studied the brain in three cases of dehydration, and found proliferative inflammatory changes limited to the interbrain. The histologic observations in all three cases were essentially the same. The second case differed in that meningeal cellular infiltration was present, restricted to the tuber cinereum. The changes are described as follows: There was diffuse cellular infiltration into the interbrain; the cells belonged chiefly to the neuroglia type, but mononuclear, and occasionally polymorphonuclear, leukocytes were also found. The vessels of the area of the brain involved showed marked congestion with leukocytes. The author is of the opinion that these changes are inflammatory, and of infectious origin. The character of this peculiar encephalitis is overwhelmingly proliferative.

The rôle that the interbrain plays in the water metabolism of the body has been demonstrated in many clinical and experimental observations. The exact associations between the nervous centers included in the interbrain and the water metabolism is not yet clear, particularly as the function of different endocrine glands, chiefly that of the pituitary gland, complicates matters.

In dehydration one is dealing with a disturbance of water metabolism. The pathologic changes in the cerebral centers associated with water metabolism suggest a pathogenetic connection. The author admits that three cases do not constitute conclusive evidence. The future must show whether or not all cases of dehydration are associated with diencephalitis, or whether there are cases in which no changes in the interbrain are demonstrable.

That the pathologic changes should be peculiarly limited to the interbrain is of course surprising, but analogous observations exist in other infectious inflam-

matory changes of the central nervous system, such as the elective changes in poliomyelitis and in lyssa.

It is admitted that the encephalitic foci could be the result of a nonspecific infection secondary to dehydration, but the histologic picture speaks rather against such an assumption. The changes are altogether different from those of infectious encephalitis. Possibly, the character of the virus is responsible for this peculiarly limited exudative leukocytic reaction, with the result of a glia cell proliferation. It is conceivable that biochemical factors play a rôle in this peculiar type of reaction. It has been shown by Schwarz that the tissue reaction to pyogenic organisms may be changed to that of agranulocytosis by a protein-rich and water-restricting diet. The author points out that clinical phenomena indicating involvement of the central nervous system are not lacking in dehydration. Convulsions and comatose states, as well as rigidity of the neck are frequently met with.

It is mentioned that the water-holding ability of the tissue is under the influence of the pituitary gland.

The administration of solution of pituitary in dehydration has proved valuable in the experience of a pediatrician working in association with the author.

In conclusion, it is again emphasized that the localization of the pathologic changes in the area of the brain that plays an acknowledged rôle in water metabolism speaks for a causal connection between encephalitis and dehydration.

RAPPAPORT, New York.

THE FIBRIN FILM IN THE CEREBROSPINAL FLUID IN THE DIAGNOSIS OF TUBERCULOUS MENINGITIS. J. AMMERSCHLÄGER, München. med. Wchnschr. **77**: 1190 (July 11) 1930.

The formation of a fibrin film in the cerebrospinal fluid of patients with meningitis has been considered characteristic of a tuberculous infection. The author found a similar film formation in the spinal fluids of three patients convalescing from meningococcic meningitis. The film was indistinguishable from that found in fluids of patients with tuberculous meningitis. The formation of fibrin film may be observed more frequently after the acute stage of meningitis has passed and the character of the spinal fluid has changed to that seen in chronic meningitis. The formation of a fibrin film can no longer be considered characteristic of tuberculous meningitis.

BRAHDY, Mount Vernon, N. Y.

FAMILIAL AMYOTROPHIC LATERAL SCLEROSIS WITH MARKED DIMINUTION IN THE SIZE OF THE CORPUS CALLOSUM. G. KREYENBERG, Ztschr. f. d. ges. Neurol. u. Psychiat. **123**:400, 1930.

Kreyenberg reports the cases of three members of one family with amyotrophic lateral sclerosis. All three became ill in the fourteenth year. Two of the cases were studied pathologically. Besides the well known changes of amyotrophic lateral sclerosis, there was a marked decrease in the size of the corpus callosum with a loss of cells in the area centralis and area heinbica.

ALPERS, Philadelphia.

A CASE OF PRECOCIOUS PUBERTY CAUSED BY A HYPOPHYSEAL TUMOR AND COMBINED WITH VON RECKLINGHAUSEN'S DISEASE. H. F. DE VRIES, Nederl. tijdschr. v. geneesk. **74**:2001 (April 19) 1930.

The author describes an interesting case of precocious puberty combined with excessive growth and with von Recklinghausen's disease (brown spots on the skin and a neurofibroma of the sole, in a girl aged 9 years. Pubertas praecox and excessive growth may be symptoms of hyperfunction of the hypophysis. The neurologic symptoms pointed to the existence of a hypophyseal tumor. Besides

the symptoms mentioned there existed dystrophia, adiposogenitalis and a decrease of 25 per cent in the basal metabolism.

The combination of precocious puberty and von Recklinghausen's disease may be explained in three ways: 1. One disease was present, namely, neurofibromatosis. In this case a neurofibroma would have developed in the hypophysis. Such a tumor does not give rise, however, to hyperfunction of the pars glandularis of the hypophysis. 2. There was a hypophyseal tumor combined with secondary neurofibromatosis, as described by Parhon and Stocker and by Starck. 3. There is no relation between hypophyseal tumor and the neurofibromatosis, but a general degenerative construction is demonstrated by the simultaneous occurrence of a neurofibroma and a disturbance of the internal secretion. Thus the condition present was related to the dystrophia ontogenetica Recklinghausen of Starck.

In the case described a definite explanation cannot be given. It is, however, the first case in which increased hypophyseal function, caused by an enlargement of the hypophysis and accompanied by von Recklinghausen's disease, is described.

VAN CREVELD, Amsterdam, Holland.

CEREBRAL PARALYSIS IN CHILDREN. C. SCHAAP, Nederl. tijdschr. v. geneesk. **74**:2225 (May 3) 1930.

Cerebral paralysis in children may be divided into two large groups: congenital paralysis and paralysis produced at a later age by different causes. The author made a study of cerebral paralysis in 107 patients (73 boys and 34 girls). He found that boys predominate among patients with cerebral paralysis and that this proportion is also found in mentally defective children. The cause of this proportion is unknown. In agreement with Siegmund and others it is thought to be probable that birth trauma has an important significance in the origin of these diseases. Of the cases of acquired paralysis, a large percentage occurs during the first years of life.

VAN CREVELD, Amsterdam, Holland.

Diseases of the Eye

A CASE OF CORRECTOPIA. A. A. KNAPP, Am. J. Ophth. **13**:141 (Feb.) 1930.

A Porto Rican boy, aged 5, whose personal and family history was irrelevant, showed eccentric pupils placed temporally and somewhat superiorly. The nasal side of each iris was arranged in radiating folds and appeared to be stretched toward the pupil. To the temporal side of each pupil was a band of iris tissue. Over the temporal portion of the pupillary area of each cornea was a vertical linear opacity in which the iris was adherent. Tension in the right eye was 85; in the left eye, 70 (McLean).

REESE, Philadelphia.

A RARE CONGENITAL ABNORMALITY OF THE EYE. IDA MANN, Brit. J. Ophth. **14**:321 (July) 1930.

The clinical history and photographs of the case described were furnished by J. N. Duggan, Bombay. The patient was a Hindu girl, aged 4 months. In place of the left eyeball there was a slightly movable, pedunculated, rounded swelling, 2 inches (5 cm.) in diameter. Posteriorly it was attached to a fibrous pedicle, about three fourths of an inch (1.9 cm.) in diameter. The normal eyelids nearly encircled the stalk just behind the posterior surface of the tumor. The surface covering of the mass resembled skin which passed imperceptibly into the conjunctiva covering the orbital cavity and the stalk.

The posterior pole was not obtained for histologic study. The mass itself was composed of fibrous tissue containing areas of fat showing myxomatous degeneration in places. The sclera and choroid were normal in structure. There was no trace of lens, anterior chamber, iris stroma or ciliary muscle. The

greater part of the mass was covered with pigmented skin. There was no trace of conjunctiva. The tumor was an aberration of differentiation of the mesoblast lying between the optic cup and the surface ectoderm. It must have begun to arise very early, as it had inhibited the growth of the lens entirely. The other accompanying deformities (skin instead of conjunctiva, faulty retinal differentiation and absence of the iris) were secondary to this primary fault and can be explained as attempted adaptations to altered environment.

This case belongs to that group of congenital fibrolipomas of the cornea which arise by an aberration of mesoderm at about the fourth week of development. According to Stargardt, they are true congenital anomalies and should not properly be classed as new growths. From a pathologic point of view, they belong to the group of monophyletic teratoblastomas, as they arise primarily from the aberration of one germ layer only. The skin and abortive retina are merely changes in surrounding structures secondary to the primary anomaly. The three cases of the same nature hitherto recorded are those of Swanzy and Leber, Hanke and Stargardt.

ZENTMAYER, Philadelphia.

AMAUROSIS IN INFANTS. P. G. DOYNE, Practitioner **125**:174 (July) 1930.

In this brief but well written paper, the author classifies the possible causes of amaurosis as follows: (1) conditions in which the eye itself is affected; these include (*a*) albinism, (*b*) cataract and (*c*) choroidoretinitis; (2) conditions due to defect of the brain; these are mainly due to mental deficiency.

The writer also describes amaurotic family idiocy. He mentions, in addition, temporary amaurosis, sometimes noted in infants.

Several cases are given from the author's own experience illustrating the various abnormalities noted.

SAPPINGTON, San Francisco.

DOUBLE PRIMARY OPTIC ATROPHY IN A BOY AGED 6½ YEARS. T. H. WHITTINGTON, Proc. Roy. Soc. Med. **23**:1001 (May) 1930.

A boy, aged 6½ years, showed double primary optic atrophy. On examination the disks were white and clear cut, but the blood vessels on them and in the fundus appeared to be normal. The condition had become progressively worse with a tragic loss of sight. No cause was found for the optic atrophy.

WILLIAMSON, New Orleans.

PHLYCTENULAR KERATOCONJUNCTIVITIS AND ALLERGY. G. LOBBONI, Ann. di ottal. e clin. ocul. **58**:28 (Jan.) 1930.

The author gives a review of the literature, including the experimental production of phlyctenules by tuberculin, horse serum and other proteins. He found the tuberculin test to be nearly always positive in these cases. Several cases are reported in which repeated intradermal tests caused the appearance of new phlyctenules. In one case the phlyctenules developed during convalescence from measles, but a Pirquet reaction was positive. In one patient with a negative Pirquet reaction symptoms of pulmonary tuberculosis developed later; still later the Pirquet reaction was positive. The same change from a negative to a positive Pirquet reaction was seen in another case, this observation being interpreted by the author as a change from a stage of anergy to one of hyperallergy in a tuberculous patient. Sixteen patients were tested by tuberculin and various other proteins. Most of them were positive to tuberculin and a number to horse serum, but very few to the other substances.

In rabbits given subcutaneous injections of horse serum and then tuberculin subconjunctivally, phlyctenules developed; the same occurred when the procedure was reversed. It did not occur when other substances, such as a nonspecific milk preparation and gonococcus vaccine, were used.

The author concludes that although in most cases tuberculosis is present elsewhere in the body and is usually the cause of phlyctenulosis, some cases are undoubtedly free from tuberculosis and the phlyctenules are produced by some other agent. Such a process is seen in cases of blepharitis. From the number of patients reacting positively to horse serum as well as to tuberculin, it seems that an allergy to tuberculin is often accompanied by allergy to horse serum.

GIFFORD, Omaha.

CONUS TEMPORALIS INVERSUS. W. LOHMANN, Arch. f. Augenh. **100-101**:853, 1929.

The author describes two cases in which the optic papilla showed a dehiscence on the temporal side just inside the choroidal crescent. He discusses the origin of these as a developmental tendency ("Entwicklungs Tendenzen"), the importance of which he has stressed in the origin of myopia.

ADLER, Philadelphia.

CLINICAL EXPERIENCES IN THE OPERATIVE TREATMENT OF CONGENITAL CATARACT. D. KLARE, Arch. f. Augenh. **102**:165 (Dec.) 1929.

This is a monographic treatment of congenital cataracts as observed in the ophthalmological clinic of Jena University during the last ten years. All forms of cataract other than traumatic are dealt with. The author found that in 74 per cent of the cases in which operations were performed, useful vision was obtained. Without operation 57 per cent of the patients could not be accepted in the normal school. Serious complications were found in only 2 of 106 eyes on which operations were performed: in one case, detachment of the retina, and in the other, phthisis bulbi. There was no loss of any eye through infection. The value of various methods of operation is described.

ADLER, Philadelphia.

A CASE OF UNILATERAL HYPOPLASIA OF THE OPTIC NERVE IN AN OTHERWISE NORMAL GLOBE. CARL VELHAGEN, Arch. f. Augenh. **102**:382 (Dec.) 1929.

The author describes the appearance of the optic nerve in a child, aged 9 years. Both eyes were normal except for the right papilla, which was only from one-ninth to one-tenth the size of the left papilla, which was normal. The optic foramen on the right side was about 1 mm. smaller in diameter than the left. No difference in the macula could be seen in either eye with red-free light.

ADLER, Philadelphia.

MULTIPLE OCULAR LESIONS DUE TO STRONG COMPRESSION OF THE THORAX. NICOLAU, Soc. Român. de oftal., Bucuresti **11**:98 (Dec.) 1929.

A boy, aged 15, who had fallen down between an iron gate and a lift, was drawn out in an unconscious state, with severe epistaxis. Ophthalmoscopy after eight days revealed marked conjunctival hemorrhages and a slight dilatation of the retinal veins; retinal edema surrounded the retinal vessels. The pathogenesis of the ocular lesions was explained by the passive venous stasis due to the compression of the thorax.

BLATT, Tagu-Mures, Roumania.

ACUTE SUPPURATIVE DACRYO-ADENITIS CAUSED BY STAPHYLOCOCCI. C. JONESCU, Soc. Român. de oftal., Bucuresti **11**:99 (Dec.) 1929.

A boy, aged 14, showed swelling of the right palpebral region, pain and fever. There were several furuncles over the body. The lacrimal gland protruded markedly into the conjunctival sac. Slight exophthalmos and downward deviation of the globe were present. The paranasal sinuses were intact; a blood culture was negative. Fluctuation occurred after three days. An incision was made

and the patient recovered. The pus contained staphylococci. Acute suppurative dacryo-adenitides are rare; the case in question was a blood-borne infection. The furunculosis was considered as the point of origin.

BLATT, Tagu-Mures, Roumania.

Surgery and Orthopedics

SOME NEUROSURGICAL PROBLEMS OTHER THAN TUMORS AND ABSCESSES. H. W. WILLIAMS, New York State J. Med. **30**:631 (June 1) 1930.

Every child with spina bifida should undergo a surgical operation unless there is nervous tissue in the sac. If the latter condition exists, the child cannot be expected to be normal and should be denied operation. Patients without the normal sphincter reflex and those with paralysis of the legs are questionable subjects for operation.

The best time for operation depends on the condition of the skin over the sac. If it is normal, operation may be delayed, but if the skin shows signs of breaking down, the operation should be performed without delay.

AIKMAN, Rochester, N. Y.

INTRACRANIAL TUMORS OF CHILDHOOD. LOYAL DAVIS, Wisconsin M. J. **29**: 429 (Aug.) 1930.

In 153 cases of intracranial tumors in the author's series there were 14 children under 15 years of age. Most of the tumors in these cases were midline cerebellar (subtentorial) and were classified as medulloblastomas of the fourth ventricle.

Persistent attacks of projectile vomiting, especially with change of posture, alternating with severe suboccipital headache, pain and tenderness are important early symptoms. Disturbed visual activity with symptoms referable to the optic nerve, hydrocephalus with separating suture lines and Macewen's sign develop on pressure. Nystagmus is not common.

Conservative surgical measures with decompression offer relief and comfort for many months. Much is to be hoped from excision by electrosurgical methods.

JANNEY, Milwuakee.

CONGENITAL DISLOCATION OF THE KNEES TREATED BY MANIPULATION. GAWAD HAMADA, Brit. M. J. **2**:141 (July 26) 1930.

A girl, aged 16 days, was brought for treatment for double congenital dislocation of the knees. The knees were hyperextended on the thighs, but could not be flexed. Manipulation was started on the right knee first. The limb was placed on a malleable posterior splint and massaged daily; manipulation was ordered, and after a short time the splint was changed to a malleable anterior splint. The treatment was then given twice weekly for the first month and once weekly later, without anesthesia.

Then the other knee was manipulated in the same way, but was found to be more troublesome owing to eversion of the leg. After eight months' treatment, the child could be supported on her limbs, the knees being stable.

ROYSTER, University, Va.

TWO UNUSUAL CASES OF INTUSSUSCEPTION. EVELEEN LYLES and FLORENCE WHITROW, Brit. M. J. **2**:181 (Aug. 2) 1930.

A boy, aged 14, had all the symptoms of acute intussusception. An operation revealed intussusception of the ileo-ileal type, which became ileo-colic. After reduction a mass could be felt through the intestinal wall. This was excised. The tumor was found to be a typical gumma. A Wassermann reaction was negative.

The second patient, a boy, aged 12, had acute appendicitis. At operation the appendix was found to be acutely inflamed and the site of an intussusception, the tip having invaginated itself almost to the base of the appendix. Recovery was uneventful.

ROYSTER, University, Va.

INJURIES OF THE ELBOW IN CHILDREN. ROBERT JONES, Practitioner **125**:179 (July) 1930.

Jones presents a splendid paper on injuries of the elbow in children, a fairly common emergency. He emphasizes the prime importance of roentgen examination. His practical observations on differential diagrams of injuries of the elbow are clear cut. He describes fractures, sprains and dislocations, and he discusses the treatment and after-care for each injury

The paper includes some excellent illustrations which demonstrate the various deformities shown on the roentgenogram. The author gives a splendid discussion of the most common complications, i. e., nerve lesions, ischemic palsy and myositis ossificans. He also describes the prophylaxis and treatment for each condition.

SAPPINGTON, San Francisco.

FLATFOOT IN CHILDREN. R. C. ELMSLIE, Practitioner **125**:195 (July) 1930.

Flatfoot, as it develops in young children, is discussed in detail. Methods of prophylaxis and treatment are presented. As the author states, "it apparently represents a trivial deformity, but if left uncured may produce trouble in later life."

The use of altered shoes and proper exercises give satisfactory results in most cases, the main difficulty being the long time required for correction.

SAPPINGTON, San Francisco.

CLEFT PALATE. JOHN FRASER, Practitioner **125**:203 (July) 1930.

Fraser presents an excellent discussion of cleft palate, beginning with the embryologic explanation of the defect and the morbid anatomy involved, and then devotes ample space to the consideration of treatment. He feels that the opportune time for operation in most cases is at the age of about 18 months.

His description of the preoperative care, the history of the various types of closure and the postoperative regimen gives an excellent idea of the importance of each detail involved. From his own experience with 104 cases, the author states that complete closure was achieved in 47 per cent. There were minor defects of healing in 35 per cent; in 15 per cent the resultant error involved a third or more of the suture line, and in 3 per cent the entire suture line gave way.

As to functional results, particularly with reference to speech, in 12 per cent speech became relatively normal, in 25 per cent it was marred by the addition of superadded sounds, and in 63 per cent articulation was persistently defective. He emphasizes the paramount importance of training in breathing and in phonetics by a qualified instructor in order to increase the opportunity for satisfactory functional results.

SAPPINGTON, San Francisco.

INTUSSUSCEPTION IN THE INFANT: OPERATION IN FOURTEEN CASES; ONE DEATH. MARCEL FÈVRE, Bull. Soc. de pédiat. de Paris **27**:398 (July) 1929.

Fourteen patients ranging in age from 3 months to 3 years were operated on for intussusception. There was but one death. The group comprised seven boys and seven girls. Possible etiologic factors are discussed from clinical and anatomic points of view. The signs and symptoms are reviewed. Roentgenologic examination after a barium enema was tried in two instances without yielding any valuable information. An early appropriate surgical procedure with careful postoperative treatment gives the best results.

BENJAMIN, Montreal, Canada.

INTERMITTENT INTUSSUSCEPTION IN AN OLDER CHILD. J. HALLÉ, V. BUREAU and J. PATEL, Bull. Soc. de pédiat. de Paris **27**:403 (July) 1929.

A boy, aged 10 years, had repeated seizures of abdominal pain as his chief complaint. An erroneous diagnosis of tuberculous peritonitis had been made on two occasions. The tuberculin reaction, which had not been obtained previously, proved to be negative even when repeated four times. Dysentery was then thought to be the probable diagnosis as some blood appeared in the stools. Later the patient was believed to have intestinal obstruction, a diagnosis confirmed by roentgenologic examination after a barium enema. He was operated on, four months after his first admission to the hospital, and an ileocecal intussusception was found. This was corrected, and the intestine was fixed by suture to the parietal peritoneum. The child recovered.

BENJAMIN, Montreal, Canada.

CONGENITAL DIAPHRAGMATIC HERNIA IN AN INFANT. VIRGILIO GUISTINIAN and DOROTEA ESTIU, Arch. argent. de pediat. **1**:553 (Aug.) 1930.

Congenital diaphragmatic hernia was found in an infant, aged 3 months; it had apparently existed almost since birth. Attacks of asphyxia with severe cyanosis were an early symptom. Dyspnea was almost constant, accompanied by a dry cough. There was continual constipation.

At autopsy, a diaphragmatic hernia was found. A large part of the omentum, intestines and stomach and a portion of the liver were found in the left thoracic cavity. The heart was displaced far to the right and there was complete collapse of the left lung.

SCHLUTZ, Chicago.

MALIGNANT RENAL TUMORS IN CHILDHOOD. ERNESTO P. TRUCCO, Arch. de hosp. de niños Roberto **1**:123 (June) 1930.

Carcinoma is the most frequent renal tumor found in childhood. According to the author, it accounts for from 40 to 50 per cent of all malignant renal tumors of childhood. The tumor has been found in the fetus. It is generally unilateral but bilateral occurrence has been reported. Boys seem to be affected more than girls. The inferior pole of the kidney is more frequently involved than the upper. The earliest possible nephrectomy offers the only hope. Life may be prolonged for about five years in 25 per cent of the cases if operation is performed early. Roentgen therapy is effective in the early stages of the disease and causes marked improvement in the general condition and a diminution of the tumor. Such results, however, are only temporary.

SCHLUTZ, Chicago.

TWO CASES OF COXA PLANA. A. INOSTROZA, Rev. chilena de pediat. **1**:226 (May) 1930.

Two children, aged 10 and 11 years, respectively, had coxa plana, the left hip being involved in both cases. Considerable improvement was noted in roentgenograms after immobilization and ultraviolet therapy.

SANFORD, Chicago.

DIFFICULTIES IN THE RECOGNITION AND TREATMENT OF INTUSSUSCEPTION. R. J. HARRENSTEIN, Nederl. tijdschr. v. geneesk. **74**:1752 (April 5) 1930.

The symptoms of intussusception are striking, but the diagnosis becomes difficult owing to the absence of the most typical symptoms (passage of blood by rectum, palpable tumor in the abdomen); symptoms of intoxication, which appear when the intussusception has existed for a long time, may also give rise to difficulties in the diagnosis. The author gives an illustration of these difficulties in an extensive description of forty-one cases. Early recognition of the condition is necessary. The difficulties in the reduction of the intussusception are only partly dependent on the length of time the intussusception has existed. Reduction

was accomplished easily in cases in which the symptoms had existed for three days; in two cases resection had to be performed after the symptoms had been present for 6 and 30 hours, respectively. In the ileocolic form, which occurs chiefly in young children, the difference in the difficulty of reduction are explained by the variations in the structure of Bauhin's valve.

VAN CREVELD, Amsterdam, Holland.

INSULIN IN THE TREATMENT OF SLOWLY HEALING WOUNDS. M. LÉVAI, Orvosi hetil. **74**:358 (April 19) 1930.

Wounds that show a tendency to slow healing, and small ulcers of the skin were treated locally with insulin. Gauze soaked in a small amount of insulin was applied to the surface of the wound with a few strips of adhesive. The result of this treatment was a quick and powerful granulation. Fresh wounds can also be stimulated by insulin. The insulin probably acts on the connective tissues; there is no elective action on the epithelium. There is practically no absorption through the granulation tissue, or it is in such small quantities that no clinical symptoms can be noted. Insulin can also be applied in dilution, without seeming to lose its effectiveness.

ZENTAY, St. Louis.

Miscellaneous

REPORT OF THE TECHNICAL CONFERENCE ON BCG. M. LEON BERNARD, M. J. & Rec. **132**:121 (Aug. 6) 1930.

A conference was held at the Pasteur Institute in Paris from Oct. 15 to 18, 1928. In this conference three commissions took part, composed respectively of bacteriologists, clinicians and veterinarians. Questions of common interest were considered in plenary session; others were studied by one or another of the three commissions. The presiding officer of the conference was Dr. E. Roux, director of the Pasteur Institute. The conclusions of these three commissions are given fully in the report.

WILLIAMSON, New Orleans.

A STUDY OF INFANT MORTALITY IN THE SOUTHERN STATES. BAIRD U. BROOKS, South. M. J. **23**:870 (Oct.) 1930.

A higher infant mortality rate prevailed in the southern states from 1924 to 1929 than in any other states of the Union. There was a decidedly higher mortality rate in the larger cities of each of the southern states studied than in other cities of similar size and widely separated.

The authors believe that intelligent care is the chief factor in reducing infant mortality. The Well Baby Clinic seems to be one of the most effective factors in reducing this mortality.

SCHLUTZ, Chicago.

MEDICAL ASPECTS OF THE NURSERY SCHOOL. BERTHA T. HAESSLER, Wisconsin M. J. **29**:504 (Sept.) 1930.

The nursery school, which is of English origin and has developed since the World War, is of definite value in the formation of early health habits and in the education of parents. Such schools, of which there are now eighty-five in the United States, best handle average children from 2 to 4 years of age in small groups (a school in Milwaukee enrolls twenty children). Routine physical examination and mental tests are performed. By the vigorous exclusion of children who are ill, acute infections are as infrequent as in the home. The hours from 9 to 3 include routine bathroom training, nap periods, a luncheon hour and free play periods. The parents are shown and taught how to avoid faulty habit training, which is most important at this early age. Problems rarely develop and when present are usually amenable to this plan.

ENLARGEMENT OF SEVERAL JOINTS (CAUSATION?). DAVID NABARRO, Proc. Roy. Soc. Med. **23**:1103 (June) 1930.

A boy, aged 8 years had been well till he was 11 months old, when he had an attack of dysentery, after which the joints became swollen. His mother had syphilis, but both the mother and the patient gave a negative Wassermann reaction. Roentgenograms of the joints showed no disease of the bones or joints. Twelve cubic centimeters of fluid were aspirated from the knee joints, but no organism of any kind was found in the fluid. The condition did not respond readily to antisyphilitic treatment.

WILLIAMSON, New Orleans.

A MAJOR PROBLEM IN MENTAL HYGIENE. K. ISEMANN, Rev. internat. de l'enf. **9**:463 (June) 1930.

In this extensive article the director of the Children's Sanatorium of Nordhausen presents his reactions to the prevailing methods of conducting classes in mental hygiene. He feels that there are two objectives to be kept in view: therapy and social adjustment. Individual treatment takes precedence over any consideration of abstract justice, in the types usually encountered in institutional work. If the child can be weaned from his antisocial attitude, secondary reactions are usually readily conquered, but the pupil then becomes dependent too largely on his environment and is apt to lose self-reliance. If more abrupt methods are employed, however, an attitude of rebellion is engendered, and the child is prone to relapse. This constitutes the chief dilemma in mental hygiene; its solution depends largely on the capacity and experience of the instructor who must alternately exercise firmness, patience and supreme tact.

AMESSE, Denver.

THE THEORETICAL PRINCIPLES OF THE ACTION OF BRINE BATHS. RÖCKEMANN, Arch. f. Kinderh. **90**:201 (May 24) 1930.

Röckemann believes that besides the external stimulation arising from peripheral capillary dilatation and contraction in alkaline baths, there is somewhat the same parallel found in protein therapy. In other words, the reaction from the bath is a stimulation that in turn stimulates protective mechanisms, like the reaction of a tuberculous child to tuberculin.

SANFORD, Chicago.

REACTIONS OF VIOSTEROL. A. STEIGMANN, Kolloid-Ztschr. **45**:165 (June) 1928.

In tests with viosterol, sulphurous acid fuchsin gives a positive reaction and ammoniacal silver oxide is reduced; the reduced silver remains, however, in the colloidal form and does not form a mirror. Viosterol is either an aldehyde or an unsaturated ketone. It probably acts as a protective colloid; hence, possibly irradiation has been accompanied by polymerization to a resin. A ketone group $>C:C:O$ would give these reactions. With irradiation in carbon dioxide a longer time is required to give equally positive reactions

KUGELMASS, New York.

CAN CONSTITUTIONAL ANOMALIES BE CURED IN CONVALESCENT HOMES? H. LANGER, Monatschr. f. Kinderh. **48**:116, 1930.

If convalescent homes are to have any effect on the child's constitution (and the author believes that the only hope of influencing a child's constitution is through such treatment), the patients must stay in them much longer than is the present custom. In addition, children must be admitted at a younger age than at present.

GERSTLEY, Chicago.

TREATMENT FOR CONSTIPATION IN INFANTS AND CHILDREN. A. F. HECHT, Wien. klin. Wchnschr. **43**:534 (April 24) 1930.

Hecht reviews the causes of constipation in infants and children and briefly summarizes the treatment. The causes of constipation may be atresia of the rectum in the new-born, Hirschsprung's disease and other malformations of the intestinal tract. In his experience breast-fed children are often constipated. He also cites the example of the hunger or starvation stool. To correct this condition he recommends the Czerny-Kleinschmidt butter-flour mixture.

A diet containing too much milk, with the absence of other foods, may also cause constipation. For this he recommends Keller's malt soup. On the other hand, a one-sided protein diet with a great deal of meat and egg and without enough roughage will produce constipation. For these children he recommends coarser vegetables, fruits, nuts and bran.

The misuse of enemas and suppositories will sometimes induce constipation. The author also states that with tetany he has found a spasm of the sphincter. For this condition he recommends the use of a belladonna-papaverin suppository and the administration of an oil by mouth. In advanced rickets constipation is common, combined with meteorism. In the beginning of acute febrile diseases of all kinds constipation is common. This is probably explained by a loss of water from the body and a disturbance of the vegetative nervous system. Hecht points out that the layman often places the "cart before the horse," by blaming the constipation for the fever. Diseases of the central nervous system may cause constipation by affecting the abdominal musculature. In chronic constipation in which it is necessary to resort to a drug, Hecht advises the use of the various oils and emulsions of oil and agar, in conjunction with suitable dietary regulation.

A. F. ABT, Chicago.

THE AVERAGE VALUES AND THE BASIS FOR THE EVALUATION OF SOME FURTHER BODY MEASUREMENTS IN CHILDREN (CIRCUMFERENCE OF HEAD, SITTING HEIGHT AND RELATIVE STEM LENGTH). W. KORNFELD, Ztschr. f. Kinderh. **49**:64, 1930.

By calculation from anthropometric material of his own, and by comparison with the results of other authors, Kornfeld obtained mean values for the circumference of the head, sitting height and stem index (the ratio of the sitting height to the standing height). On the basis of these adjusted mean values and of adjusted mean values of the coefficients of these three measurements, tables have been laid out which make possible the classification of each individual value found.

EMERSON, Boston.

MEDICAL AND SOCIAL CARE OF PSYCHOPATHIC CHILDREN IN SWEDEN. I. JUNDELL, Acta pædiat. **10**:1 (Aug. 18) 1930.

The author believes that the study and treatment of mental problems in children can best be carried out in special clinics that have hospital as well as dispensary facilities and that are attached to, and under the direction of, the pediatric divisions of the larger university clinics. Only in this way can the necessary cooperation between pediatrician and psychiatrist be attained and the patient be studied with proper emphasis on all phases of his condition. Such organizations should not attempt to carry out the entire program of treatment in all cases single-handed, but should act as clearing-houses, sometimes supervising home care and at other times taking the responsibility for commitment to other institutions.

MCINTOSH, New York.

Society Transactions

NORTH PACIFIC PEDIATRIC SOCIETY

Twenty-Third Semi-Annual Session, Seattle, July 12, 1930

W. B. PATRICK, M.D., *President, in the Chair*

Morning Session, Children's Orthopedic Hospital

CHRONIC CARBOHYDRATE INDIGESTION. DR. D. B. LEITCH, Edmonton, Alberta (read by secretary).

Five boys, aged from 5 to 8 years, displayed a clinical syndrome marked chiefly by anorexia, pallor, abdominal discomfort, cramps, overexercise, fatigability, constipation and stationary weight. In each case, the author obtained a history of excessive intake of carbohydrate, principally in the form of candy. Improvement promptly followed the restriction of starches and sugars, together with enforced periods of rest. To control the pain, tincture of nux vomica and tincture of belladonna were employed.

TRAINING THE CHILD TO EAT. DR. C. E. HUNT, Eugene, Ore.

Nutritional needs may vary as much as 40 per cent in children of the same age. To explain a given case of anorexia, one must first find or exclude chronic infections (diseased tonsils and teeth, pyelitis, tuberculosis, etc.). Other causative factors to be considered are teething, overfatigue, overexcitability, rickets and a diet too rich in fat.

DISCUSSION

DR. J. I. DURAND: A diet high in protein, similar to that used in treating patients with celiac disease, has been useful in selected cases of anorexia.

DR. A. S. MCCOWN: A child's craving for parental solicitude is often one of the principal causes of anorexia.

DR. N. W. CLEIN: Physicians frequently fail to recognize the normal variations in the appetites of infants.

DR. JOSEPH BRENNEMANN: In orphanages, where children eat together, anorexia is practically unknown.

PEDIATRIC CLINIC. DR. JOSEPH BRENNEMANN, Chicago.

Mediastinal Tumor.—A girl, aged 3 years, suffered from loss of weight and anorexia for several months. Severe attacks of anginoid pain had also occurred. The heart tones were loud on the right side of the chest, indicating cardiac displacement. A roentgenogram showed a smooth round shadow occupying the inner two thirds of the field of the left lung. Several deep roentgen treatments had no effect on the tumor.

Operation for removal of this type of tumor is justified. A rather unusual tumor of the mediastinum in children is the neuroganglioma, which is benign and occasionally removable. (NOTE.—Since the presentation of this patient, operation was attempted. A large mediastinal mass was removed, which the pathologist has not yet diagnosed. The patient died approximately twenty-four hours after operation.)

Tuberculous Cervical Lymphadenitis.—A boy, aged 3 years, presented suppurative enlargement of the cervical lymph nodes and a low grade fever. A history of tuberculosis in his family was not obtained. The Mantoux test gave positive results. A roentgenogram of the chest showed shadows suggestive of tuberculosis of the hilus glands.

Tuberculosis of the cervical glands is seldom encountered in this, in contrast to previous, decades.

Vomiting in the New-Born Infant.—An infant, aged 6 days, had vomited in a projectile manner since birth. Visible peristalsis was not present. Following the administration of phenobarbital, the vomiting ceased.

Many infants vomit in this manner during the early days of life. The cause is unknown, but it may be related to cerebral irritation resulting from passage through the birth canal. It is especially apt to occur after difficult deliveries, and it usually ends spontaneously in a few days. In this infant, duodenal obstruction must also be considered — in which, however, one would expect to find considerable bile in the vomitus. Fluoroscopic observations should not be depended on too much in deciding for or against operation on an infant with suspected pyloric or intestinal obstruction.

A Constitutional Anomaly of Unknown Classification.—An only boy, aged 17 months, was the product of an easy labor, but was cyanotic at birth. The cyanosis disappeared, but the infant nursed poorly for several days. The skull was poorly ossified. There was pronounced spasticity of the arms, the hands and the legs, which gradually disappeared. The anterior fontanel closed at about 1 year of age. Sitting and walking were retarded. At the time of presentation, the child had a peculiar, mature appearance. The head was narrow, and the brow overhanging. The left half of the chest was larger than the right. The hair and skin were normal.

This patient presents some of the features of oxycephaly or "türmschadel." The condition is probably a developmental anomaly of the skull, rather than a primary cerebral disturbance.

Nonhemolytic Streptococcus Septicemia.—A boy, aged 7 years, suffered from an acute respiratory infection in December, 1929. Tonsillectomy had been performed a year previously. In June, 1930, he began to have fever and epistaxis. Anemia soon developed, and he was hospitalized, and a blood transfusion performed. The fever, which reached 103 F. on admission, subsided within a few days. There remained, however, a pronounced diastolic murmur in the region of the mitral valve.

The assumption of valvular endocarditis on the basis of a murmur of the heart is not always justified. In many of these patients, one finds merely a dilated mitral ring at autopsy. In low grade septicemic infections, recovery does occasionally occur, contrary to the general belief.

Chronic Nephritis with Edema.—A Japanese girl, aged 12 years, was hospitalized two years previous to presentation for acute hemorrhagic nephritis. She again entered the hospital in June, 1930, on account of general anasarca. Albuminuria was constant and pronounced. Symptoms of vomiting and stupor, bordering on uremia, were frequent. On June 28, the blood urea was 117 mg. per hundred cubic centimeters, and the creatinine, 4.3.

In the beginning, this patient had an acute case of hemorrhagic nephritis. In such a primary attack, fluids should not be restricted even in the presence of generalized edema. On the basis of a large number of clinical experiments with controls, a German investigator was unable to determine any deleterious effects from feeding meat to children with acute hemorrhagic nephritis. In the so-called "nephrosis," a focus of infection may be the etiologic factor, but one is frequently not successful either in locating or in eradicating it.

Afternoon Session, Boulevard Inn

TWO CASES OF FOCAL INFECTION. DR. R. G. HALL, Portland.

Two patients in whom acute tonsillitis displayed an unusually protracted course were described. Typhoid and paratyphoid fever had been excluded by agglutination tests. The maxillary and other sinuses apparently were not involved. In both patients the fever promptly subsided, following a few injections of autogenous vaccine prepared from cultures from the throat, together with ultraviolet irradiation.

DISCUSSION

Dr. M. S. Miles: In a case similar to those of Dr. Hall, two intramuscular injections of whole blood brought the prolonged fever to an abrupt termination.

Dr. J. I. Durand: There are some proponents of tonsillectomy in the acute stage of tonsillitis, but as a rule it is safer to wait until the acute infection has subsided before operating.

Dr. Joseph Brennemann: Tonsillectomy should not be performed during the course of acute tonsillitis.

Dr. E. D. Kanaga: In tonsillectomy, the snare is a safer instrument to use than the devices which compress the tonsil, since the latter are liable to force bacteria into the blood stream.

Dr. R. G. Hall: I use a vaccine containing 500,000,000 bacteria per cubic centimeter. Starting with from 0.1 to 0.2 cc., the dose is increased 0.2 cc. at each injection. For the associated swelling of the cervical lymph glands, I employ a heat lamp, which is used for forty minutes three times daily.

The Use of Roentgenograms in the Interpretation of Conditions of the Chest in Children. Dr. Joseph Brennemann, Chicago.

The author delivered a lecture, illustrated by a large number of lantern slides of roentgenograms of the chest, illustrating his experiences with diseases of the chest in infancy and in childhood from the standpoint of the roentgenogram. The basis of his report was a series of observations made on children at the Children's Memorial Hospital, Chicago, in which roentgenographic observations had been correlated with clinical observations. In 176 cases which came to autopsy, roentgenograms were made of the lungs before and after removal from the body, and finally minute anatomic dissections were made.

In the past, the diagnosis of pulmonary tuberculosis has frequently been made by roentgenologists without justification, because they have not considered clinical evidence in conjunction with roentgen observations. Fifty per cent of patients with miliary tuberculosis have negative roentgenograms of the chest; the other 50 per cent show the characteristic "snowflake" appearance of the lungs. The acute bronchopneumonia or interstitial pneumonia may, however, give a closely similar picture. Most of the linear shadows seen on the film of a normal chest are not due to bronchi, but to blood vessels, since the latter have greater volume and density than the air passages. The shadow on the roentgenogram most likely to represent a tuberculous lesion is a triangular one in the hilar region, which is continuous with the border of the heart. Primary lesions, especially early ones, may cast no shadow. Calcification of tuberculous lesions is rare in early infancy, but has been seen in the second year.

Epituberculosis, which was first described by Eliasberg, is probably an allergic reaction in the pulmonary tissue surrounding a tuberculous focus. Very little fever is present in these patients.

Pyopneumothorax is easily missed in a roentgenogram taken with the child in a prone position. When the film is made with the patient sitting up, the fluid level is self-evident.

Massive collapse of the lung appears in the roentgenogram as a diffuse unilateral shadow with displacement of the cardiac shadow toward the affected side. It may be due to any condition, accompanied by shallow breathing and stasis of the bronchial secretions.

Roentgenograms of the chest in several other interesting clinical conditions were shown. They included ganglioneuroma of the mediastinum; ovarian cyst with metastasis of the lung; ecchinococcus lesion of the liver, with extension to the mediastinum; lymphosarcoma; cyst of the lung, occupying nearly the entire thoracic area on the left side; serous pericarditis secondary to pneumococcic pneumonia, and empyema.

DISCUSSION

DR. S. G. HENRICKE: I recently observed a patient with epituberculosis following an attack of erythema nodosum.

INFANTILE TETANY AND VIOSTEROL. DR. NORMAN W. CLEIN, Seattle.

The dosage of viosterol should be calculated according to the infant's own requirements. One cannot feel secure in prescribing supposedly adequate doses of viosterol to some infants, because symptoms of deficiency in calcium may develop while they are receiving them. Two cases are reported to illustrate this point.

CASE 1.—An infant, aged 20 months, had rickets at the age of 7 months, and was clinically cured during the next two months. He was given 10 drops of viosterol daily for seven months, and subsequently tetany developed. This was relieved by increasing the amount of viosterol to 30 drops daily.

CASE 2.—A girl, aged 3½ years, was well until the age of 38 months, when she had three severe convulsions within two months. She improved on 15 drops of viosterol daily, but another convulsion occurred one month later. Cure was effected by the use of 30 drops daily.

This report illustrates the fact that tetany occurred in two patients, one having had at least 10 drops of viosterol daily for seven months prior to the development of tetany, the other having had from 10 to 15 drops daily for more than two months before active symptoms developed.

Treatment with Viosterol

	Before	After Increasing Dose
Case 1:		
Blood calcium	7.6	11.5
Blood phosphorus	4.3	7.7
Case 2:		
Blood calcium	8.7	13.0
Blood phosphorus	5.2	6.8

Not sufficient clinical experience over a long period of time has been accumulated to warrant giving the same dose of viosterol to each infant, any more than experience would warrant feeding every infant the same food from similar cans. Prophylactic doses of from 12 to 20 drops daily would be more adequate in the Pacific Northwest than the usual dose of 10 drops. Every infant should be considered as an individual, and the dose of viosterol should be calculated according to the type, weight, rapidity of growth and development of that particular infant.

CARDIOSPASM IN INFANCY: REPORT OF A CASE. DR. HARRY C. OLMSTED, Seattle.

An infant girl vomited in a projectile manner from the first day of life. On the sixth day the vomiting became suddenly worse, with symptoms of complete intestinal obstruction. At operation, the obstruction, although not definitely located, was apparently relieved by the surgeon's manipulations. On examination, the pylorus was found to be normal. Thereafter, the projectile vomiting recurred. No improvement followed the use of thick cereal feedings and concentrated formulas, and the administration of atropine and phenobarbital. The fifth week, fluoroscopic examination revealed a definite stasis of barium mixture in the lower portion of the esophagus. Feedings by a tube were instituted, with the result that within a week the vomiting had practically ceased.

This infant probably suffered from spasm in several localities of the gastrointestinal tract, but principally in the pylorus and the esophagus. Fluoroscopy should be performed in every stubborn case of vomiting, when the infant has not responded to routine treatment, in order to rule out the possible existence of a cardiospasm.

CHICAGO PEDIATRIC SOCIETY

Regular Meeting, Oct. 21, 1930

A. H. PARMELEE, M.D., *President, in the Chair*

AN UNUSUAL TYPE OF GENERALIZED BONY DEFORMITY. (PRESENTATION OF PATIENT.) DR. HERMAN MEYER and DR. JOSEPH BRENNEMANN.

A patient from the outpatient department of the Childrens' Memorial Hospital who had been under observation for seven years, with an unusual type of osseous deformity, was presented. The essential pathologic changes involved all of the bones except those in the head, particularly the epiphyses of the long bones, producing a peculiar gross deformity of the body unlike anything in the experiences of the presenters. They had been able to find only one other report in the literature of a case of apparentlly the same condition.

DISCUSSION

DR. JOSEPH BRENNEMANN: We have observed this child for a period of seven years and have become more and more puzzled. It early became evident that this was not a manifestation of rickets. I think that we know little more than we did at first. When I saw the pictures in the case reported in a French journal, I was at once impressed with the fact that this boy looked like those children as much as they looked like each other. I have never seen anything like it, and I think that the condition is sui generis. I think that the essential thing is that there is a fairly general lack of transition from cartilage to bone.

The pelvis is most interesting. This 7 year old boy has no more bony formation, or perhaps not as much, as an infant of 9 months.

The question is whether we should treat the deformity of the legs as we would ordinarily treat such a deformity in a rachitic patient. I am afraid that in doing so we might make a bad matter worse.

DR. C. A. ALDRICH: I wonder whether Dr. Hodges said anything about the possible connection between this case and osteitis fibrosa cystica. It occurred to me that this disease occurring in an infant might produce these changes. Several cases have been reported of osteitis fibrosa cystica associated with parathyroid hyperactivity, and I wonder if this may have some bearing in this case.

DR. A. H. PARMELEE: The case is interesting. I happen to have under observation a child whose condition is very similar to that in this case, and I will present her at a later meeting. My patient is about 4 years of age, with practically the same deformity. Mentally she is normal. She came to me at the age of 18 months, with a diagnosis of severe rickets. Roentgenograms seemed to show chondrodystrophia. Once I tried to show that there might be various stages of chondrodystrophia, that the disturbance of cartilage might not always be of such degree as to produce the same type of dwarfism. This case may not be one of chondrodystrophia, but merely because it does not follow along the same lines and fit in the pigeon hole of what one has in mind for that disorder, does not mean that it may not be chondrodystrophia. I believe that there may be manifestations of chondrodystrophia that differ from those seen in the typical chondrodystrophic dwarf.

DR. JOHANNA HEUMANN: How much viosterol is the child getting?

DR. HERMAN MEYER: Ninety drops a day.

DR. JOSEPH BRENNEMANN: I feel that this case differs greatly from the reported cases of osteitis fibrosa cystica. Whether or not one should call the condition chondrodystrophia may be a question, but in many ways it is the antithesis of what is commonly called chondrodystrophia. If this case is one of chondro-

dystrophia, or achondroplasia, there are two types of chondrodystrophia. Dr. Chandler has suggested that it be called chondrodysplasia. I think that more cases will be seen, but I believe that they will be found rarely.

CAUSES OF DEATH AND DISEASES OF CHILDREN AS FOUND IN A THOUSAND CONSECUTIVE NECROPSIES (INAUGURAL THESIS). DR. I. M. EPSTEIN.

The records of 1,000 consecutive necropsies, covering a period of eight and a half years and constituting 48 per cent of the deaths at the Children's Memorial Hospital during that period, were reviewed.

The data were presented mainly in tabular form, including a table of the causes of death which gave the distribution as to age and sex, a table of meningitis with the distribution as to age and causative bacteria, a table of tuberculosis with the distribution as to age and type of infection, a table of congenital anomalies with age distribution, a table of acquired heart disease showing the frequency of involvement of the different valve leaflets and of the pericardium, a table of septicemia showing the frequency of involvement of the different viscera and the causative bacteria and a table of the neoplasms showing the type and distribution of metastases.

The comment on the tables was mainly explanatory.

DISCUSSION

DR. CLIFFORD G. GRULEE: Even at the risk of unduly prolonging the discussion, I should like to ask a question or two.

If I heard correctly the statement of the essayist it was to the effect that in his opinion lobar pneumonia was not nearly so frequent in these children as bronchopneumonia. One cannot draw a conclusion about the incidence of lobar pneumonia in children from necropsy observations. I think that he brought out that point well, but I wish to take issue with him as to the frequency of lobar and bronchopneumonia as clinical entities. I am speaking of the clinical picture of lobar and bronchopneumonia. Brennemann will say that we cannot distinguish between the two. I suppose in a certain percentage of cases that is true, but in cases in which bronchopneumonia is so massive that it is mistaken for lobar pneumonia, it is usually seen at the necropsy table.

I have no figures to support my contention, but I know when diagnoses made in the ward in the last few years were reviewed, it was found that judged clinically lobar pneumonia was as frequent as bronchopneumonia. There was nothing in the report that discounts that conclusion, because bronchopneumonia is so much more fatal than lobar pneumonia that the fact that there were 130 cases of death from bronchopneumonia and only 30 from lobar pneumonia does not mean much of anything.

I was much surprised to see that there had been forty-three deaths from empyema. I suppose that they all occurred previous to two years ago.

DR. JOSEPH BRENNEMANN: I think that Dr. Grulee should remember that this is an autopsy report and not a clinical report. Dr. Epstein has emphasized that it has no bearing on the incidence of disease but on the incidence of pathologic conditions found at the Childrens' Memorial Hospital at necropsy. The reason why there was no more cases of lobar pneumonia is because patients with lobar pneumonia do not die so frequently as do those with bronchopneumonia. I think that that is the usual clinical experience. We used to teach that lobar pneumonia was the common clinical disease also in children. I think that the situation has changed a great deal since my earlier days. Earlier statistics were based largely on statistics from the Babies' Hospital in New York and, of course, young institutional children died, then as now, of bronchopneumonia, not lobar pneumonia.

In reply to Dr. Grulee, most of the deaths from empyema occurred prior to two or three years ago. There are not so many deaths from empyema now.

DR. H. E. IRISH: What are the criteria that Dr. Epstein uses in the postmortem diagnosis of lobar pneumonia and bronchopneumonia?

DR. I. M. EPSTEIN: In reply to Dr. Grulee, there was no intent to draw conclusions as to the relative frequency of lobar pneumonia and bronchopneumonia. As was emphasized in my paper, these figures are of children that have died. The diagnosis of bronchopneumonia at postmortem examination is made from the gross observations when possible, by the scattered distribution of the lesions and by the evident different stages of development of the pneumonic lesions. Often when the distribution is lobar, a positive diagnosis can be made only from the characteristic appearance of the histologic sections.

THE BLOOD PICTURE IN WHOOPING COUGH (SPECIAL REFERENCE TO EARLY OBSERVATIONS). DR. L. W. SAUER and L. HAMBRECHT, Evanston, Ill.

This article will be published in full in a later issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN.

DISCUSSION

DR. JESSE R. GERSTLEY: In the initial and terminal leukopenia which Dr. Sauer discussed, was there any change in the differential count?

DR. GEORGE F. MUNNS: I was particularly interested in the leukocyte counts. I have done many counts on these patients, and it is quite true that it is often difficult to make an early diagnosis. I think that several things have to be considered when one is studying the blood count in whooping cough. The general opinion is that a high leukocyte count is found in whooping cough. While this is true in established cases, this symptom is often not found in the early stages, but in most instances there is definite change in the differential count. I have here figures on the cases of seventy children who had whooping cough. All of these counts were taken between the tenth and fourteenth day of the cough, according to the history. Of course, the cough may have been going on several days longer or several days less than the parents said.

Most of these children were of the school age. I found that in over 85 per cent there was a lymphocyte count of 50 per cent or more. I think that most of the observers of blood counts are rather well agreed that the lymphocytes do not go over 50 per cent after about the fifth year. On the average they drop below 50 per cent about the fifth year. It is interesting to see in the tables of some observers that before the fifth year they dropped to around 20 or 30 per cent, but in Abt's counts and in those of some others this does not occur before the fifth year. If the child has been coughing from ten to fourteen days and a lymphocyte count above 50 per cent is found, it should make one suspicious that pertussis is the cause.

DR. M. L. BLATT: Does Dr. Sauer think that there was anything in his treatment that influenced the count?

DR. LOUIS SAUER: No vaccine was given; in severe cases the patients received two small doses of phenobarbital and quinine daily for a few weeks. No medication was given during the catarrhal and decline periods.

As to the differential counts: Dr. Munns' observations agree with ours at the end of the catarrhal or early paroxysmal periods. In the initial leukopenia period the lymphocytes did not predominate; when the counts went up the lymphocytes increased markedly, and in the terminal leukopenia the lymphocytes were again not so high. In infants this difference was less pronounced than in older children. For example, on the third day of the catarrhal period a 6 year old child showed a white cell count of 4,200 with 48 per cent polymorphonuclears; on the fourteenth day the white count had reached 21,300 with only 14 per cent polymorphonuclears.

Book Reviews

GRUNDLAGEN UND ENTWICKLUNGSGESCHICHTE DER KINDLICHEN NEUROSE. By DR. ERICH BENJAMIN. Price, 9 marks. Pp. 141. Leipzig: Georg Thieme, 1930.

If in the past thirty years psychology and medicine have had little in common but mutual distrust, the causes of this undesirable state must be sought for in a wide divergence of methods and interests. The physician could see no gain in accompanying the psychologist through an adolescent period of extreme subjectivism which his craft had traversed a century before. Nor could he — mindful of his responsibilities to higher interests than the vagaries of the individual human being — ignore the asocial character which the teachings of the psychologist had assumed. Hence it was that the physician, and in particular the pediatrician, withdrew to the fireside of the rule "by the thumb" in matters psychologic and let the winds of doctrine rage at will without. Benjamin's brochure is the first psychology that the reviewer has read which is written from the physician's standpoint and which meets the physician's needs. Whether Benjamin's conception of the neurosis will ultimately be accepted is at present not important; decisive is the fact that the book is both a symbol for the new age in psychology and a powerful stimulus to further studies by medically trained and minded psychologists.

In this review an attempt will be made to sketch the mere skeleton of Benjamin's views, leaving it to the interested reader to discover that the method of approach which Benjamin has adopted is probably as important as the interpretation of his observations. He believes that the neurosis of the child is in all its protean manifestations the expression of one factor — a retardation in the normal pace of development which permits infantile traits to be carried on into a later stage of childhood. The development of the neurotic child is patchy; the harmony of the different mental, spiritual and physical characteristics is destroyed. The powers of observation and assimilation, the memory and intellectual interest develop without, however, the concomitant increase in perseverance, concentration, logical faculty and self-confidence. The gross muscular abilities increase, but the child still retains the infantile excessive and purposeless motor phenomena, as well as the crudeness, ineffectiveness and instability of the infant's motor control. One sees in this that the neurosis is not merely a behavior problem, but that it involves the physical statics and dynamics of the body. The fundamental difficulty, however, Benjamin finds, is the failure to progress from the rigid egocentric world of the infant to the social world of comradeship and mutual forebearance. Here the author clashes with the teachers whose prime object seems to have been to develop the child's personality at the cost of all other factors. Benjamin insists on the importance of social adaptability, and in the pursuit of this end he regards a measured display of authority as justifiable.

Eighty-five per cent of the neurotic children of all ages have a history of behavior problems which stretches back into infancy. Hence Benjamin believes that at this age the foundation of the neurosis is laid. A disturbance so fundamental may well be determined by idiotypic factors, i. e., inheritance in the strictest sense of the term. In the discussion of this question Benjamin again gives evidence of his ability to think quantitatively. Many characteristics of the neurotic child, such as physical abnormalities and differences between male and female neurotic children, make it absolutely necessary to assume that there is an anlage which is idiotypic. This, however, like all psychic traits, is indeterminate. The fate of this anlage is fixed within wide bounds by the paratypic factors of environment.

The first contact of the infant with its surroundings set the direction of reactions, the effects of which will be discernible even in the later years of childhood. The factors that have a deleterious effect need not be mentioned here; again Benjamin insists on the importance of leading the young child away from the normal egocentric trend of the infant. He is skeptical of the success of any but symptomatic treatment in the older child, for by this time the elasticity which is a prerequisite has decreased and only rarely will one be able to penetrate behind the organized wall of defense which the child, now conscious of the value of its neurosis, will have erected. Benjamin discourses at some length on the development of a social service for the neurotic persons of tender age; he advises the organization of kindergartens, homes, etc. I believe that such methods will reach only a small percentage of the cases; one may be permitted to be skeptical of the practical realization of the theoretical values. Much more important is Benjamin's other suggestion: The reeducation of the educators. If the pediatrician can carry into the homes of his patients his ideal of mental hygiene with the same persuasiveness that the psychologists have employed, the lever will have been placed on a fulcrum from which medicine can attack the behavior problem. For in the end the child must be educated through the parent and one must agree with Goethe's couplet: "Man könnt erzogene Kinder gebären, Wenn die Eltern erzogen wären." (Educated children could be born, if the parents had been educated.)

THE CHEST IN CHILDREN. By E. GORDON STOLOFF, M.D. Volume XII. Annals of Roentgenology. Edited by James T. Case, M.D. Price, $15. Pp. 432, with illustrations. New York: Paul B. Hoeber, Inc., 1930.

This volume is really an atlas of roentgenograms of the chest in children in health and in disease. The illustrations are supplemented by a brief explanatory text that is well written, concise and to the point. The illustrations themselves are excellent, and each has a full descriptive legend. Not only the typical conditions, but the variations from the usual, are portrayed. The effect of technic on the picture itself is explained, and the variation of direction of the rays is shown by the result on the picture.

Many cases are illustrated in series, showing the progress of the disease as pictured on the plates.

Beginning with the bronchi, and especially stressing the effect of foreign bodies, the volume contains excellent plates of conditions affecting also the lungs and the pleura. Tuberculosis is well presented.

The cardiac disturbances are not shown, but conditions affecting the mediastinum, the wall of the chest, the diaphragm and other structures are well treated.

The book is exceedingly well published and will fill a long felt need.

MANUAL OF THE DISEASES OF THE EYE. By CHARLES H. MAY, M.D. Thirteenth edition. Price, $4. Pp. 444, with 374 original illustrations. New York: William Wood & Company, 1930.

This is the thirteenth edition of a popular textbook for undergraduate students and for the general practitioner. It has been brought up to date by the inclusion of valuable information on the microscopy of the living eye and in the presentation of such matters as the recently advocated cautery of the eye in detachment of the retina. The author has maintained the original size of the book by omitting controversial subjects, stating facts that are regularly conceded by the better practitioners.

The size of the volume prohibits much detailed discussion of pathology; this subject is considered from the clinical aspect, and the illustrations in color are so profuse that a most excellent general view of each disease is given.

The discussion of the subjects "Symptoms" and "Treatment" is given in such simple language that one readily understands the thoughts of the author.

The headings, paragraphing, spacing and type of print add to the pleasure of reading a well organized and dependable textbook.

HANDBOOK OF PEDIATRIC PROCEDURES. By F. S. SMYTH and E. I. M. IRVINE-JONES. Cloth. Price, $2.50. Pp. 212. New York: The Macmillan Company, 1930.

This book is a brief description of the methods for the study and treatment of disease in children. It is divided into two parts. Part I deals with diagnosis. Especial points of pediatric value are given in the history and physical examination. The laboratory diagnosis gives a brief but workable description of practically all the tests of value. Part II deals with therapy. The chapter on dietetics could have been made of greater value if the metric system had not been used throughout. This rather handicaps it as a book for rapid reference for the practicing pediatrician. Biologic therapy and physical therapy are well discussed. The material on drug therapy contains a good table of dosages and some good suggestions for various diseases. A chapter each is devoted to the introduction of fluid into sick children and procedures such as lavage, gavage and lumbar and cistern puncture. The chapter on emergency treatment is excellent.

This book is unique in that it covers the subject well in a short space. It is written in outline form and is easy of access. It should have a place in every pediatrician's library.

CONGENITAL CLUB-FOOT. By E. P. BROCKMAN, F.R.C.S. Cloth. Price, $4. Pp. 110, with 92 photographs and diagrams. New York: William Wood & Company, 1930.

This is the most satisfactory book that has ever been written on congenital clubfoot. The author has selected everything that is essential to his subject and has stated it clearly. He has omitted the immaterial things.

The text consists of a historical survey of the literature, the nature of the deformity, the normal and pathologic anatomy, the etiology and the methods of treatment with results.

The author emphasizes the fact that the deformity resists correction, because of the dislocation of the scaphoid downward and mediad, and he gives details of his open operative technic to correct the dislocation and thereby correct the deformity.

The book is printed on good paper with good type.

ARTIFICIAL SUNLIGHT. By M. LUCKIESH, D.Sc. Price, $3.75. Pp. 254, with 65 figures and 8 plates. New York: D. Van Nostrand Company, 1930.

This book might be termed a textbook on radiation. The effects of radiant energy have been coordinated with the physics of the subject, making a combination that should be helpful both in biologic research and in therapeutic practice. The important subjects discussed include: solar radiation, effects of spectral energy, reflection of ultraviolet radiation, transmitting mediums, infra red radiation, permanency of materials, incandescent solids, measurement of ultraviolet radiation and electric arcs. The final chapter deals with the utilization of lighting for the best effects. This book is interesting and well written, and should be of value not only to the physician interested principally in electrotherapy, but to any one who wishes a thorough knowledge of the field of radiant energy.

LA VACCINATION CONTRE LA TUBERCULOSE PAR LE B C G. By K. CHAUSSINAND. Paper. Price, 38 francs. Pp. 195, with 6 tables. Paris: Gaston Doin, 1930.

This book is a compact résumé of the practical and experimental work done on B C G vaccination. The first part deals with animal experimentation and the second part with experiments on man; the third part contains a complete bibliography. The subject is discussed fairly, fully and completely. The results of the various investigators in all countries are set down as completely as possible. The author's conclusions are that infants can be vaccinated by mouth, subcutaneously, intramuscularly and intraperitoneally without danger. The efficacy of vaccination against tuberculosis has been demonstrated.

EXPERIMENTELLE TUBERCULOSEFORSCHUNG UND PHARMAKOHISTOLOGISCHE UNTERSUCHUNGEN. By DR. SEIGO FUNAOKA. Paper. Pp. 120, with illustrations. Gyoto: Universität Kyoto, 1930.

This book contains collected papers from the Anatomical Institute of the Kaiserlichen Universität, Kyoto. There are eight papers on experimental tuberculosis and six on pharmacology.

STUDIES FROM THE DEPARTMENT OF PEDIATRICS, WASHINGTON UNIVERSITY SCHOOL OF MEDICINE AND THE ST. LOUIS CHILDREN'S HOSPITAL. Ninth series. Pp. 80. St. Louis, 1929.

This book consists of a collection of sixteen articles of pediatric interest, from the members of the Department of Pediatrics of Washington University.

Directory of Pediatric Societies

INTERNATIONAL

International Pediatric Congress

President: Dr. George Frederic Still, 28 Queen Anne St., London, W. 1.
Place: London. Time: 1933.

NATIONAL

American Medical Association, Scientific Assembly, Section on Diseases of Children

Chairman: Dr. C. A. Aldrich, 723 Elm St., Winnetka, Ill.
Secretary: Dr. Alfred A. Walker, Highland Plaza Apartments, Birmingham, Ala.
Place: Philadelphia. Time: June 8-12, 1931.

American Academy of Pediatrics

President: Dr. I. A. Abt, 104 S. Michigan Ave., Chicago.
Secretary: Dr. C. G. Grulee, 310 S. Michigan Ave., Chicago.
Place: Atlantic City, N. J. Time: June, 1931.

American Child Health Association

President: Hon. Herbert Hoover, Washington, D. C.
Secretary: Dr. Philip Van Ingen, 125 E. 71st St., New York.

American Pediatric Society

President: Dr. Philip Van Ingen, 125 E. 71st St., New York.
Secretary-Treasurer: Dr. Howard Childs Carpenter, 1805 Spruce St., Philadelphia.
Place: Edgewater Gulf Hotel, Edgewater Park, Miss. Time: April 15-17, 1931.

Association of American Teachers of the Diseases of Children

President: Dr. Jacob V. Greenebaum, 19 W. 8th St., Cincinnati.
Secretary: Dr. Ralph M. Tyson, 334 S. 21st St., Philadelphia.
Place: Philadelphia. Time: June 8-12, 1931.

Children's Hospital Association of America

President: Dr. Howard Childs Carpenter, 1805 Spruce St., Philadelphia.
Secretary-Treasurer: Miss Bena M. Henderson, Milwaukee Children's Hospital, Milwaukee.

Canadian Society for the Study of Diseases of Children

President: Dr. E. A. Morgan, 160 Bloor St., Toronto, Ont.
Secretary-Treasurer: Dr. George E. Smith, 244 Bloor St., W., Toronto, Ont.

SECTIONAL

Central States Pediatric Society

President: Dr. A. Graeme Mitchell, 345 McAlpine Ave., Cincinnati.
Secretary: Dr. A. H. Parmelee, 310 S. Michigan Blvd., Chicago.
Place: Cincinnati. Time: Fall, 1931.

Southern Medical Association, Section on Pediatrics

Chairman: Dr. D. Lesesne Smith, 188 S. Church St., Spartanburg, S. C.
Secretary: Dr. Ludo von Meysenbug, 3439 Prytania St., New Orleans, La.
Place: New Orleans. Time: November, 1931.

STATE

Alabama Pediatric Society

President: Dr. Hughes Kennedy, Jr., Highland Plaza Apts., Birmingham.
Secretary-Treasurer: Dr. John W. Simpson, 1117 S. 22nd St., Birmingham.

Georgia Pediatric Society

President: Dr. W. N. Adkins, Medical Arts Bldg., Atlanta.
Secretary-Treasurer: Dr. E. N. Gleaton, 212 E. Gaston St., Savannah.

Louisiana State Pediatric Society

President: Dr. R. A. Strong, 1551 Canal St., New Orleans.
Secretary-Treasurer: Dr. Suzanne Schaeffer, Chailie Bldg., New Orleans.

Oklahoma State Pediatric Society

President: Dr. Carroll M. Pounders, 210 W. 10th St., Oklahoma City.
Secretary: Dr. C. E. Bradley, Medical Arts Bldg., Tulsa.
Place: Oklahoma City. Time: May, 1931.

South Carolina Pediatric Society

President: Dr. M. W. Beach, 126 Meeting St., Charleston.
Secretary-Treasurer: Dr. Julian P. Price, The McLeod Infirmary, Florence.

Texas Pediatric Society

President: Dr. L. O. Godley, Medical Arts Bldg., Fort Worth.
Secretary-Treasurer: Dr. P. E. Luecke, 4105 Live Oak St., Dallas.

Virginia Pediatric Society

President: Dr. W. B. McIlwaine, Petersburg.
Secretary: Dr. J. B. Stone, 2042 Park Ave., Richmond.

LOCAL

Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. O. L. Goehle, 15701 Detroit Ave., Lakewood, Ohio.
Secretary: Dr. W. C. Fargo, 8314 Euclid Ave., Cleveland.
Place: 2009 Adelbert Road. Time: Four meetings, from September to May.

Academy of Medicine, Toronto, Section of Pediatrics

President: Dr. Gladys Boyd, 56 DeLisle St., Toronto.
Secretary: Dr. Lawrence Murray, 1870 Bloor St., W., Toronto.
Time: November 17, December 15, February 16 and March 15.

Bronx Pediatric Society

President: Dr. Joseph Golomb, 496 E. 175th St., New York.
Secretary: Dr. E. Leonard Benjamin, 2229 Valentine Ave., New York.
Place: Concourse Plaza, 161st St. and Grand Concourse. Time: Second Wednesday of each month, except June, July, August and September.

Brooklyn Pediatric Society

President: Dr. Benjamin Kramer, 6 Pierrepont St., Brooklyn.
Secretary: Dr. Lambert Krahulik, 172 Clinton St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Last Wednesday of each month, except June, July and August.

Central New York Pediatric Club

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Fourth Thursday of October, January and April.

Chicago Pediatric Society

President: Dr. Arthur H. Parmelee, 310 S. Michigan Ave., Chicago.
Secretary: Dr. Bert I. Beverly, 8 S. Michigan Ave., Chicago.
Place: City Club. Time: Third Tuesday of each month.

Detroit Pediatric Society

President: Dr. Allan L. Richardson, 651 Fisher Bldg., Detroit.
Secretary: Dr. Joseph A. Johnston, Henry Ford Hospital, Detroit.
Place: Children's Hospital of Michigan. Time: No fixed date; approximately once a month.

Fulton County Medical Society, Pediatric Section (Atlanta, Ga.)

Chairman: Dr. Lee Bivings, Exchange Bldg., Atlanta.
Secretary: Dr. William Kiser, Medical Arts Bldg., Atlanta.
Place: Academy of Medicine, 32 Howard St. Time: Second Thursday of each month from October to April, 8 p. m.

Memphis Pediatric Society

President: Dr. Kinsey M. Buck, 1024 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. R. B. McCormick, 1074 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month.

Milwaukee Pediatric Society

President: Dr. H. O. McMahon, 84 E. Wisconsin Ave., Milwaukee.
Secretary: Dr. F. R. Janney, 2018 E. North Ave., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

Nebraska Pediatric Society

President: Dr. H. B. Hamilton, 434 Aquila Court Bldg., Omaha.
Secretary: Dr. George L. Clark, 1817 Vinton St., Omaha.
Place: As announced by committee. Time: Second Thursday of each month from October to June, inclusive, 6 p. m.

New England Pediatric Society

President: Dr. Grover F. Powers, New Haven, Conn.
Secretary: Dr. Gerald Hoeffel, 319 Longwood Ave., Boston.
Place: Boston Medical Library. Time: October, January and March.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Hugh Chaplin, 39 E. 75th St., New York.
Secretary: Dr. John P. Caffey, Babies' Hospital, 167th Street and Broadway, New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

North Pacific Pediatric Society

President: Dr. Eber D. Kanaga, Townsend Bldg., Tacoma, Wash.
Secretary: Dr. Homer T. Clay, Washington Bldg., Tacoma, Wash.

Northern California Pediatric Society

President: Dr. Edward B. Shaw, 384 Post St., San Francisco.
Secretary-Treasurer: Dr. Lloyd Hardgrave, 384 Post St., San Francisco.
Place: Various teaching schools. Time: Monthly.

Northwestern Pediatric Society

President: Dr. E. S. Platou, 730 La Salle Bldg., Minneapolis.
Secretary: Dr. F. G. Hedenstrom, 218 Lowry Bldg., St. Paul.
Place: University Campus and Rochester, Minn. Time: Winter, Spring, Summer, Fall.

Philadelphia Pediatric Society

President: Dr. Ralph M. Tyson, 334 S. 21st St., Philadelphia.
Secretary: Dr. John D. Donnelly, 115 Bryn Mawr Ave., Bala-Cynwyd, Pa.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

Pittsburgh Pediatric Society

President: Dr. David H. Boyd, 200, 9th St., Pittsburgh.
Secretary: Dr. Theodore O. Elterich, 724 Highland Bldg., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate months from October to April, inclusive.

Richmond Pediatric Society

President: Dr. Basil B. Jones, 2618 Grove Ave., Richmond, Va.
Secretary-Treasurer: Dr. John S. Weitzel, 3103 W. Franklin St., Richmond, Va.
Place: Westmoreland Club, 601 E. Grace St. Time: First Thursday of each month (other than during the summer).

Rochester Pediatric Society

President: Dr. John Aikman, 184 Alexander St., Rochester, N. Y.
Secretary: Dr. Howard F. Rowley, 176 S. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: First Friday of each month from October to May.

Rocky Mountain Pediatric Society

President: Dr. Bernard C. Dorset, 1612 Tremont St., Denver.
Secretary-Treasurer: Dr. Wilford W. Barber, 227, 16th St., Denver.
Place: Children's Hospital, Denver. Time: Third Saturday of each month from September to May, inclusive, 2:30 p. m.

St. Louis Pediatric Society

President: Dr. Gustave Lippmann, 3720 Washington Blvd., St. Louis.
Secretary-Treasurer: Dr. Katherine Bain, 3720 Washington Blvd., St. Louis.
Place: St. Louis Children's Hospital. Time: At least once a year and contingent thereafter on the arrangement of a suitable program.

Seattle Pediatric Society

President: Dr. Vernon W. Spickard, Cobb Bldg., Seattle.
Secretary: Dr. Raymond H. Somers, Cobb Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, 7 p. m.

Southwestern Pediatric Society

President: Dr. William S. Bowers, 1136 W. 6th St., Los Angeles.
Secretary: Dr. Fred L. Glascock, 1136 W. 6th St., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. E. P. Russell, Berwyn, Ill.
Secretary: Dr. John P. Parsons, 320 S. Division St., Ann Arbor, Mich.

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